"ROLE OF INTRAVAGINAL MISOPROSTOL IN INDUCTION OF LABOUR"

THESIS
FOR

DOCTOR OF MEDICINE
(OBSTETRICS & GYNAECOLOGY)

BUNDELKHAND UNIVERSITY,
JHANSI (U.P.)

2005 **NEELAM**


Dedicated
to
My Parents

CERTIFICATE

This is to certify that the work entitled ***"ROLE OF INTRAVAGINAL MISOPROSTOL IN INDUCTION OF LABOUR IN TERM PREGNANCY"*** which is being submitted as a thesis for ***M.D. (Obstetrics and Gynaecology)*** examination, 2005 under Bundelkhand university by ***Dr. NEELAM,*** has been carried out in the department of obstetrics and gynaecology. ***M.L.B. Medical College., Jhansi*** under my direct supervision and guidance. The observations recorded have been checked and verified by me from time to time.

She has put in the necessary stay in the department as per required by the regulation of Bundelkhand University

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Jhansi :

Dated : 15/10/04.

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Introduction

INTRODUCTION

The position of women in any civilization is an index of advancement of that civilization and the position of a women is judged best by the care given to her at the birth of her baby. The advances and regressions of civilization are nowhere seen more clearly than in the story of child birth.

Giving birth to a baby on one hand provides happiness to mother and entire family, but on other hand has always been darkened with pain, agony and fear of some mishap, more commonly with first confinement. For ages long, there has been no solution for the problems of prolonged labour and non progress of labour leading ultimately to great mortality and disability from infections and operations.

With the passage of time, attention is now been focused for a healthy pregnancy outcome, even if it means to initiate labour earlier than it would take place at natural events. Induction is indicated when the benefit to either mother or foetus outweigh those of continuing the pregnancy.

Induction of labour is the non spontaneous initiation of uterine contraction that result in progressive cervical effacement and dilatation with descent of the presenting part. Induction of labour should not be attempted unless there are sound obstetrics grounds for expediting the termination of pregnancy.

Induction of labour is defined as one in which "pregnancy is terminated artificially any time after the 28th weeks of gestation by a method that aims to secure delivery per via naturales." (Donald I: 1979).

Condition of the cervix is important for labour induction. Determination of suitability for elective induction is made by evaluation of Bishop Score which include dilatation, effacement, consistency and position of cervix, and station of the presenting part. Elective induction may be successfully and safely perform when the Bishop score totals 9 or more (Bishop E.H.1964).

Unfortunately women too frequently have an indication for induction of labour but with various degree of an unripe cervix. Effectiveness of induction of labour depends predominantly on duration of pregnancy and cervical status both of them correlating with sensitivity of the myometrium towards labour inducing agents.

Indications for labour induction includes post dated pregnancy, premature rupture of membranes, intrauterine growth restriction, intrauterine foetal death, congential anamoly of foetus, Rh incompatibility and maternal medical complications such as diabetes mellitus, pregnancy induced hypertension and chronic hypertention. While inducing labour, the obstetrician is attempting to induce prematurely the two interlinked components of labour: cervical ripening and uterine contractility. Cervical ripening whether physiological or pharmacological is the conversion of the rigid "cervical sphincter" associated with maintenance of pregnancy to a compliant and readily dilating structure. This allows uterine contractility to effect the birth of the fetus with comparative ease. The objective of the pharmacological induction of a physiological process is an attempt to mimic the natural process as closely as possible.

Since antiquity various methods, many bizarre and some frankly dangerous have been used in an attempt to induce labour. Initially pituitary extract was used as labour inducing agent (Hofbauer, 1941). Methods of

induction of labour include mechanical methods such as digital stretching of the cervix, stripping of membranes, hygroscopic cervical dilators, extraamniotic balloon catheters, artificial rupture of membranes, nipple stimulation to administration of smooth muscle stimulants such as castor oil (Mitri, 1985), oxytocin, prostaglandin & prostaglandin analogues. Out of these methods most acceptable medical methods for induction of labour are the use of oxytocin & prostaglandins.

In unfavorable cervix, prostaglandin preparations have proved to be beneficial (Keirse, 1993).

Oxytocin:

The role of pituitary hormones in parturition was proposed as early as the beginning of this century. In 1941, Hofbauer used pituitary extract for induction of labour.

The uterus is insensitive to oxytocin until near term when its sensitivity increases several fold & once the process of labour starts there is an increase in the gap junctions and oxytocin receptors in the myometrium. Oxytocin inhibit calcium pump resulting in increased intracellular calcium which lead to myometrial activity, increased synthesis of prostaglandins due to activation of phospholipases & increased phosphatidyl inositol hydrolase.

The oxytocin has the disadvantage of high failure rate when the cervix in unfavourable and requires monitored continuous intravenous infusion. With unfavourable cervix a high dose of oxytocin is required which may result in excessive uterine activity, foetal distress & increased risk of operative interference.

Misoprostol:

Misoprostol is a synthetic prostaglandin analogue structurally related to prostaglandin E_1 { (+) Methyl 11α , 16-dihydroxy-16 methyl-9-oxoprost- 13-en-l -oate}. It is a methyl ester of prostaglandin E_1 additionally methylated at C-16, originally manufactured for prevention and treatment of NSAIDs induced gastric ulcers by diminishing gastric acid secretion and cytoprotective action but it also has known uterotonic and cervical ripening effect and has been used "off label" for elective medical abortions, cervical ripening, induction of labour, even to treat and prevent post partum haemorrhage. Molecular weight of misoprostol is 382.5. It is water soluble and stable at room temperature due to cellulose matrix (Chuck et al, 1995).

Misoprostol is extensively absorbed and undergoes rapid deesterification to it's free acid (misoprostol acid) which is responsible for its clinical activity and is detectable in plasma. The alpha side chain undergoes beta oxidation which undergoes omega oxidation to inactive dimer and tetramer metabolites (Foote, 1995) followed by reduction of ketone to give prostaglandin F analogue.

Misoprostol acts by selective binding to EP_2 / EP_3 prostanoid receptors. PGE_1 has been shown to have a greater affinity for the receptor subtype EP_3, ($EP_3 < EP_2 < EP_1$) which is a potent activator of phospholipase C, leading to dose related increase in intracellular calcium in myometrial cells but have less affinity to EP_4 receptor, (ASBOTH, 1996). PGE_1 may cause problems precisely because it is a less potent activator of leukocytes and collagenases while being a more potent activator of myometrial cells. (Prin 1999).

T_{max} of misoprostol acid is 12 ± 3 min and halflife 20 - 40 minutes.

The bio-availability of vaginally administered misoprostol is three times higher than that of orally administered misoprostol when determined by area under curve (AUC). The markedly different AUC values are likely the result of presystemic gastrointestinal or hepatic metabolism that occur with oral but not with vaginal administration. The greater bio-availability of vaginal misoprostol may explain why intravaginal misoprostol has been reported to be more effective than oral misoprostol (Toppozada et al, 1997). The bio-availability of misoprostol is decreased by concomitant ingestion of food or antacids. Misoprostol has no known drug interactions and does not induce the hepatic cytochromic P-450 enzyme system. Misoprostol is primarily metabolized in the liver, primarily eliminated through non renal route and less than 1 percent of its active metabolite is excreted in urine. Patient with hepatic disease should receive a lesser dose, whereas dose adjustment is unnecessary for patients with renal insufficiency who do not require dialysis (Foote et al, 1995).

Adverse Effect ;

The most common gastrointestinal side effects are diarrhoea and abdominal pain. Others are nausea, flatulence, headache, dyspepsia, vomiting, Chills, shivering and fever, all of which are dose dependent, In the pregnant women being induced with misoprostol abnormal uterine contractions such as Uterine tachysystole (> 5 contractions per 10 minutes for two consecutive 10 minute periods), uterine hypersystole / hypertonus - (A contractions of 2 minutes or more) and Uterine hyper - stimulation syndrome (uterine tachysystole or hypersystole with foetal heart rate changes - such as persistent decelerations, tachycardia or reduced short term variability), may occur and these were first described with Misoprostol use at term by Mariani Neto (1988).

Uterine tachysystole rapidly resolves after subcutaneous or intravenous terbutaline injections.

Mobius syndrome (Congential fascial paralyisis) and limb defects have occurred in infants of women who have taken misoprostol during the first trimester in an unsuccessful attempt to induce abortion. Other malformations being noted are increased frequency of transverse limb defects, ring-shaped constriction of extremities, arthrogryposis, hydrocephalus, holoprosencephaly and extrophy of bladder in infants exposed to misoprostol in utero (Goldberg, 2001).

Over-dosage:

The toxic dose of misoprotol have not been determined, however cumulative doses up to 2200 microgram administered over a period of 12 hours have been tolerated by pregnant women, with no serious adverse effect. A dose of 6000 microgram of misoprostol, taken orally to induce an abortion resulted in abortion, hyperthermia, rhabdomyolysis, hypoxemia and a complex acid-base disorder. Clinical signs that may indicate an over dose are sedation, tremor, convulsions, dyspnea, abdominal pain, diarrhoea, fever, palpilations, hypotension or bradycardia. Symptoms should be treated with supportive therapy (Bond, 1994).

Misoprostol is available in the tablet form of 100 microgram and 200 microgram.

Routes of administration :

- Oral
- Sublingual
- Vaginal
- Cervical
- Rectal

In the present study conducted in the Department of Obsterics and Gynaecology of Maharani Laxmi Bai Medical College, Jhansi prostaglandin E_1 analogue Misoprostol was used vaginally for induction of labour and results were compared with oxytocin induction.


Aims
and
Objectives

AIMS AND OBJECTIVE :

- To evaluate the effect of vaginal misoprostol on cervical ripening and labour induction at term.
- To evaluate induction - active labour interval and induction delivery interval.
- To evaluate labour complications and perinatal outcome.
- To compare safety, efficacy and perinatal outcome with intravenous oxytocin induction.

Review of Literature

REVIEW OF LITERATURE

Margulies et al (1992) did two studies to corroborate the efficacy of vaginal misoprostol in inducing uterine contractions during the third trimester of pregnancy- a dose finding study and comparative trial of misoprostol and oxytocin. In dose finding study conducted on 56 pregnant women, in group I gestational age was 28-36 weeks (11 cases) and in group 2 gestational age was more than 36 weeks (45 cases). In all cases induction of labour was medically indicated. An initial dose of 50 microgram vaginally, was followed by increasing doses of 50 microgram every 2 hour until satisfactory uterine activity was achieved or maximum of total 600 microgram misoprostol. The percentage of patients delivered within 8 hours of induction was 36% in group 1 and 73% in group 2 and the average dose required was 162 microgram in group I and 188 microgram in group II. More than half of the patients responded to a single 50 microgram dose. 3 women reported diarrhoea and hot flushes, but no adverse effects on the fetus or baby were observed.

In the second study, 64 pregnant women with a single fetus and intact membranes and in whom induction was necessary for medical or obstetric reason were induced. In 33 cases 50 microgram misoprostol was given vaginally and the other 31 were given intravenous oxytocin. In misoprostol group induction was successful in 79 % cases and in oxytocin successful in 62 % cases. Induction delivery interval was 407 $\pm$ 265 minutes in the misoprostol group and 577 $\pm$ 605 in oxytocin group ($p=0.2$) side effects were not observed but polysystole was more frequent in misoprostol group (17%) than in oxytocin group (12%). No difference was found in birth weight or Apgar Scores in both groups. They suggested that misoprostol is effective in the induction of labour in the third trimester

of gestation with few side effects on the mother and no apparent adverse effect on the fetus or new born baby.

Fleteher et al (1993) conducted a double blind clinical trial in Jamaica, to determine the effectiveness of intravaginal Misoprostol in improving Bishop score, leading to an early safe vaginal delivery in whom the cervix is unripe and delivery is indicated. Out of 45 women 100 microgram of misoprostol was given in 24 women and 21 received placebo and the efficacy was measured by the increase in the Bishop score 12 hours after giving the treatment, time between insertion and delivery, the need for oxytocin and the out come of the pregnancy. The study concluded that the Misoprostol is an effective and cheap method of inducing labour in third trimester.

The change in Bishop score was 5.3 in Misoprostol compared to 1.5 in the placebo group ($p<0.001$). The mean time from insertion to delivery was 15.6 h in the former while it was 43.2 h in the placebo group

Sanchez Ramoz, Kaunitz et al, (1993). Conducted randomized trial in 1993 on labour induction with Misoprostol versus oxytocin. In this study 132 patients were randomly assigned to one of two induction groups with prior cervical ripening using Prostaglandin E2 gel. They found out that uterine tachysystole occurred more frequently in patients of the Misoprostol group (34.4%) than in Oxytocin group (13.8%) ($p<.05$). Nevertheless, no statistically significant differences were noted between the groups in intrapartum complications including uterine hyperstimulation syndrome, mode of delivery and neonatal or maternal adverse outcomes. The interval from induction to vaginal delivery was significantly shorter in the Misoprostol group (11 versus 8 hours $P= 0.004$). In 74% of patients of Misoprostol group, only one intravaginal dose was required for successful

labour induction. They concluded that intravaginal Misoprostol safely and effectively induces labour while minimizing the expense associated with intravenous Oxytocin infusion. The higher frequency of uterine tachysystole in Misoprostol group did not increase the risk of adverse intrapartum or perinatal outcomes.

Bugalho A, Bique C, (1994), assessed the effectiveness and safety of intravaginal Misoprostol for induction of labour in Intrauterine fetal death. The study design was of 72 women at 18-40 weeks of pregnancy with intrauterine fetal death, without abdominal scars, were treated with 100 micrograms of intravaginal Misoprostol. The dose was repeated every 12 hourly until effective contractions and cervical dilatation were obtained, for upto 48 hours. The mean time from induction to delivery was 12.6 hrs and only six patients (8%) required between 24 and 48 hours from initiation of induction to delivery, at the end of which all patients had been delivered. No surgical procedure or side effects were reported.

Bugalho A. et al (1995) tested the effectiveness and safety of low dose vaginal Misoprostol for induction of labour in women with late fetal death. 156 pregnant women were either induced with vaginal Misoprostol or intravenous Oxytocin infusion. Treatment outcomes were compared to cost effectiveness and safety. In the Misoprostol group none received more than 800 micrograms. In cases with Bishop scores < 6, the induction to delivery interval averaged 14.8 hours in the Misoprostol group and 31.0 hours in oxytocin group (P = 0.001). The corresponding values for women with Bishop Scores > 6 were 6.6 and 8.7 hours respectively (P=0.4). Women with intact membranes had an induction to delivery interval of 13.8 hours in Misoprostol group and 26.9 hours in oxytocin group (P=.002) and with ruptured membranes it was 7.8 and 10.5 hours

respectively. Successful induction was achieved in 81% of Misoprostol treated women at a dose of 100 microgram or less.

Bugalho A, Bique C, Bergstrom S (1995). In their study, 52 pregnant women who had labour induced by intravenous oxytocin were compared with 404 pregnant women in whom labour was induced with of vaginal Misoprostol (50-100 microgram). The induction to delivery intervals in the oxytocin and Misoprostol groups, respectively, had the following durations. With Bishop Scores <6, 24.3 Vs. 14.4 hours (p=0.002), with Bishop's score more than or 6, 10.5 Vs. 6 hours (p=0.02), with ruptured membranes 8.8 Vs 8.5 hrs (p=0.83) and with intact membranes, 19.6 Vs 13.1 hours (p=0.005). The caesarean delivery rate was 17.3% in the oxytocin group and 8.7% in the Misoprostol group (P=0.09). Maternal complications were few and drug side effects rare. They concluded that vaginal Misoprostol is a valuable and cost effective alternative to intravenous oxytocin infusion for induction of labour.

Machungo, Faundes, (1995) tested the effectiveness and safety of low dose vaginal Misoprostol for induction of labour with a live fetus. Labour was induced in 666 pregnant women with a live fetus in cephalic position who had no medical complications and no history of uterine surgery. 50 micrograms of Misoprostol was placed in posterior vaginal fomix every 12 h. for a maximum of four doses or until active labour commenced. Labour was successfully induced in all cases. The mean time from induction to delivery was 10.4 hr. The caesarean rate was 7.8%. There were 8 perinatal deaths, six of which occurred in low birth weight foetuses. The study included that vaginal Misoprostol in low doses is a remarkably efficient and safe method for induction of labour with a live fetus.

Varaklis (1995) compared Misoprostol 25 micrograms administered at 2 hourly intervals with intracervical prostaglandin E2 gel in women with Bishop scores of 5 or less for induction of labour in 80 pregnant women at term. Women who received Misoprostol experienced a significantly reduced mean time (± standard deviation) from drug administration to onset of three contractions in 10 minutes compared to prostaglandin E_2 (6.7 ± 5.8 versus 12.4 ± 9.6 hours p = 0.007) Mean time to rupture of membranes was also shorter in the Misoprostol group, 9.7 ± 5.5 versus 13.6 ± 6.8 hours (p=0.01) as was the mean time to delivery, 16.0 ± 7.7 versus 22.4 ± 10.9 hours (p=0.006). Three patients in the Misoprostol group experienced uterine hypertonus but not related foetal morbidity. The study concluded that Misoprostol is more effective than intracervical PGE_2 in bringing about labour and delivery, but further work is needed to determine the ideal dosing regimen.

Wicker R. et al (1995) demonstrated that Misoprostol are a cost effective and safe means of cervical ripening compared to Dinoprostone gels. 117 women with Bishop scores < five received either 25 microgram Misoprostol vaginally 6 hourly upto maximum of 3 doses or 0.5 milligram Dinoprostone gel cervically 6 hourly upto maximum of 3 doses. Patients treated with Misoprostol had significantly higher Bishop scores, shorter time from first dose to induction (25.7 verses 20.3 hours), lower number of doses needed and shorter time from first dose to delivery (44.2 verses 37.6 hours). No difference in intrapartum complications, caesarean section rate, postpartum complications or neonatal outcome were noted.

Windrim R, et al (1995) tested the effectiveness, safety and gastrointestinal tolerance of oral Misoprostol for induction of labour against other established protocol in 275 pregnant women, with the interval from induction to vaginal birth as primary measure. 137 women

received 50 microgram Misoprostol orally every 4 hours as needed. Dose could be increased to 100 microgram of no satisfactory progress was noted after two 50 microgram doses. The control group included 138 women induced by 0.5 milligram of Dinoprostone intracervically, 1 or 2 milligram of Dinoprostone intravaginally every 6 hours or intravenous oxytocin infusion. There was no significant difference regarding interval from induction to delivery (926 $\pm$ 521 minutes verses 909 $\pm$ 585 minutes) maternal secondary outcome measure, maternal gastrointestinal side effects and neonatal outcome. They concluded that misoprostol may be a new option for labour induction.

Kadonali et al, (1996) conducted a randomized study to compare the efficacy and safety of intravaginal and oral Misoprostol verses oxytocin / PGE_2 for third trimester labour induction in 224 pregnant women. Patient in Misoprostol group (112) received 100 microgram vaginal Misoprostol followed by 100 microgram orally every 2 hour. The oxytocin / PGE_2 group consisted of 112 patients who underwent PGE_2 cervical instillation 6 hours before continous oxytocin infusion. Induction to active phase of labour was successfully achieved in 96 women (76.8 %) in Misoprostol group vs. 86 (85.7%) in oxytocin / PGE_2 group, but the induction delivery interval was significantly shorter in misoprostol group (9.2 $\pm$ 2.4 hours) than in Oxytocin /PGE_2 group (15.2 $\pm$ 3.2 hours, $p < 0.001$). The incidence of adverse intrapartum outcomes was similar for both methods. There was higher prevalence of caesarean sections for failed induction in oxytocin / PGE_2 group than in misoprostol group (13.4 vs. 6.3 %, $p < 0.001$). An interesting finding was that rapid progression of labour when cervical dilation reached 5 cm. or more in the misoprostol group the time interval between 5 cm. cervical dilatation to delivery was only 16 $\pm$ 1.2 hours in oxytocin / PGE_2 group and 7.8 $\pm$ 2.4 hours in misoprostol group. They

observed that misoprostol is significantly more effective and acceptably safe agent for labour induction and cervical ripening than oxytocin / PGE_2 gel.

Wing DA, Paul RH (1996) compared two dosing regimens of vaginally administered Misoportol for cervical ripening and labour induction. Five hundred twenty patients were randomly assigned to one of the two dosing regimens (Misoprostol 25 microgram 3 hourly Vs 6 hourly) The average interval from start of induction to vaginal delivery was (903.3 $\pm$ 482.1 min) in the three hourly group as compared to (1410.9 + 869.1 min) in the 6 hourly group. There was a slightly higher incidence of tachysystole in the 3 hourly group (14.6%) than in 6 hourly group (11.2%). No significant difference in perinatal or maternal outcome between two groups were noted. The study concluded that misoportol is an effective agent for cervical ripening and induction of labour. Patients with the 6 hourly group required more frequently oxytocin augmentation, and had more failed inductions.

Chang CH_1 Chang FM 1997 did a randomized comparison of Misoprostol and Dinoprostone for labour induction in 60 women at term singleton pregnancy. 12 hours after drug insertion the mean Bishop Scores were significantly better in Misoprostol group compared to Dinoprostone (9.7 $\pm$ 3.1 Vs. 7.3 $\pm$ 2.5) The mean time from insertion to delivery was shorter in compared to Dinoprostone (16.5 $\pm$ 2.7 hours Vs. 25.7 $\pm$ 3.8 hours,). They concluded that Misoprostol vaginal tablet is not only an effective ripening agent and labour inducer but is also more effective than dinoprostone vaginal tablet.

Kramer RL et al (1997) conducted a randomised trial to compare the safety and efficacy of Misoprostol and oxytocin for induction of labour.

Study group included ; 35 women requiring induction were randomized to receive either intravenous oxytocin or 100 microgram Misoprostol vaginally every 4 hourly until labor was established. Greater percentage of women in the Misoprostol group had Bishop scores of 3. or less. The induction to delivery interval was significantly shorter (585 versus 885 minutes). Misoprostol group were more likely to deliver with in 24 hours of the start of induction. The total percentage of caesarean deliveries were not significantly different although was lower in Misoprostol group (8 versus 21% p=0.02). They concluded that use of Misoprostol results in shorter induction to delivery interval, reduction in rate of caesarean section but uterine tachysyctole is significantly more common with Misoprostol ($p<001$).

Leszczynska - Gorzelak B,etal (1997) conducted a study in Poland, to evaluate the safety and efficacy of intravaginal Misoprostol in cervical ripening and labour induction in term pregnancy with unfavourable cervix (Bishop score < 4). 64 women with indications for termination of pregnancy received either Misoprostol (group M, n=30) or IV infusion of oxytocin (group 0, n=34). The profile of the studied women was evaluated as regards gravidity, weight, height, maternal age, gestational age, preinduction Bishop score. There were no differences in the patients profiles (gravidity, weight, height, age, gestational age) between groups except preinduction Bishop score was lower in group M. The interval between the initiation of induction to active labour was shorter in the Misoprostol group (334.23 + 126.35 versus 610.00 + 352.14 minutes). The mean time between the initiation of induction to delivery was shorter in group M (707.69 + 341.15 versus 1025.77 + 369.16 minutes). These differences were statistically significant. 28 (93.33%) patients in the Misoprostol group delivered within 24 hours compared with 24 (70.59%)

women in the oxytocin group. 8 patients in the Misoprostol group and 8 patients in the oxytocin group had caesarean section. Labour induction was successful in 30 (100%) women in Misoprostol group compared with 24 (70.59%) patients in group O. Misoprostol thus is an effective, easy to use, cheap drug for induction of labour in women with unfavourable cervix (Bishop score < 4).

Srissomboon J. et al 1997, compared the efficacy of intracervical versus intravaginal Misoprostol in term. 100 patients with unfavourable cervix. (No significant difference was noted between intracervical and intravaginal Misoprostol in terms of Bishop score change (score 7.2 Vs. score 7.5), induction-delivery interval (17.0 hours Vs. 16.4 hours), mode of delivery and perinatal outcome). They concluded that the two routes are equally effective but practically intravaginal is better.

Toppozada et al, (1997), compared efficacy of vaginal versus oral Misoprostol for induction of labour. Induction was carried out on 40 women near term in two equal and randomized groups. Group I received vaginal Misoprostol (100 microgram) every 3 hour while group II patients were given the same dose via the oral route. The dose was doubled when no response was detected. The vaginal route of administration induced a higher success rate in a shorter time interval using a lower dose but was associated with more abnormal FHR patterns and instances of uterine hyperstimulation.

Rodrigues R. Nunes F, Tiago Diagno D et al (1998) evaluated the efficacy and safety of intravaginal Misoprostol for labour induction. In 110 women with term singleton pregnancy fractionated doses of Misoprostol were applied (50-100 microgram), every 6 hourly until a maximum of three doses or beginning of labour. The average interval ($\pm$ S.D.) from

vaginal application to the beginning of the active labour and to delivery were, respectively, 9.5 ± 5.7 hours and 14.8 ± 9.5 hours. Failed labour induction was observed in two cases (2%). Caesarean section rate was 14%. The incidence of tachysystole was 18% and hypersystole 4%, but these situations were associated with abnormal foetal heart rate pattern (hyperstimulation) in only 3%. No maternal side effects and neonatal adverse effects were noted. Intravaginal Misoprostol administration with low doses is an effective and safe method for labour induction in term pregnanceis; with or without rupture of membranes.

Wing D.A., et al (1998) conducted a randomized trial to compare the safety and efficacy of vaginally administered Misoprostol with the use of intravenous oxytocin for cervical ripening and labour induction in 38 pregnant women with prior caesarean delivery. 17 subjects received 25 microgram Misoprostol vaginally 6 hourly upto maximum of 6 doses and 21 received oxytocin. Disruption of the prior uterine incision was found in two of the 17 Misoprostol treated women. They opined that when misoprostol is used in women with previous caesareans, there is a high frequency of disruption of prior uterine incisions.

Blanchette et al, (1999) compared the safety and efficacy of vaginal Misoprostol with Dinoprostone for cervical ripening and labour induction. Study involved 81 patients induced with PGE_2 and 145 patients with PGE_1 The mean time to delivery was shorter in the Misoprostol group, there was no increased caesarean rate. Incidence of hyperstimulation was higher in dinoprostone group. There were 2 uterine rupture and one dehiscence with Misoprostol group, in 3 patients with previous caesarean delivery.

Danielion P., et al (1999) compared the efficacy of vaginal Misoprostol and Dinoprostone vaginal gel for induction of labour at term.

211 pregnant women were randomly assigned to receive vaginal Misoprostol either 50 microgram four hourly to a maximum of four doses or Dinoprostone gel 1 microgram six hourly to a maximum of three doses. Among those evaluated 105 received Misoprostol and 106 received Dinoprostone. The average duration of induction to delivery interval was shorter in Misoprostol group compared with the Dinoprostone group (14.4 hours vs, 22.9 hours, $p < 0.00001$), more women delivered after only one dose (77 % vs. 49 %, $p < 0.0001$) and within 12 and 24 hours. Need for oxytocin augmentation of labour occurred more commonly in the Dinoprostone group (47 %) than in the Misoprostol group (21 %) ($p< 0.0001$). No adverse neonatal outcome was associated with the use of Misoprostol, however women in the Misoprostol group experienced more pain in the interval between induction and being given analgesia in labour but that must be balanced against reduction in induction delivery interval.

Kolderup et al (1999) compared the efficacy and safety of misoprostol with dinoprostone for labour induction in 159 women with gestation of >31 weeks, Bishop Score < 6 and fewer than 12 contractions per hour. 81 pregnant women received 50 microgram misoprostol vaginally after every 4 hourly (maximum of 6 doses) while 78 pregnant women were given 0.5 mg of intracervical prostaglandin E_2 every six hours (maximum of 4 doses). Mean time to delivery was significantly shorter in the misoprostol group (19 hours 50 minutes) than in dinoprostone group (28 hours 52 minutes) ($p = 0.005$). Only 58 % women of misoprostol group received oxytocin augmentation, in comparison with 88% of women receiving dinoprostone ($p = 0.00002$). There was no difference in caesarean delivery rate between the groups. Misoprostol group (36 %)was associated with significantly more frequent occurrence of tachysystole than dinoprostone group (10%). 41% of women

receiving misoprostol and 17% receiving PGE_2 had late deceleration or bradycardia ($p = 0.001$) and 20% of the misoprostol group and 5% of the dinoprostone group had deliveries for fetal distress. They pointed out that misoprostol is more efficacious than dinoprostone for labour induction but either a lower dose of misoprostol or less frequent dosing of misoprostol should be considered.

Liu H.S. et al (1999) conducted a study on 89 patients to see the effect of intracervical Misoprostol on induction of labour. 50 microgram of Misoprostol was given cervically and dose was repeated very 4 hr. until adequate uterine contraction and cervical dilation were achieved. Among 89 patients, 58 had an un-favourable cervix (Bishop score < 4) and 31 had a favourable cervix (Bishop score >4). Labour was induced in all cases. Seventy two patients (81%) proceeded to spontaneous vaginal delivery and 61 (85 %) deliveries were achieved within 12 Hours The mean duration from induction to regular uterine contraction and to delivery was 483 $\pm$ 537 min in cases with Bishop Score < 4 and 79.2 $\pm$ 38.2 min in cases with Bishop Score > 4. They suggested that intracervical administration of misoprostol is effective method for induction of labour at term with no untoward side effect on mother or fetus.

Nunes F. et al (1999) in a randomized study on one hundred eighty nine pregnant women compared intravaginal misoprostol and dinoprostone for cervical ripening and induction of labour. They observed that interval from application of the initial dose to beginning of active phase of labour was 9.8 $\pm$ 5.8 hours and 14.2 + 10.2 hours ($p < 0.1$) and the interval from initial dose to delivery was 15.3 $\pm$ 9.8 hours and 19.1 $\pm$ 13.2 hours ($p = .027$) for the Misoprostol and Dinoprostone group respectively. There were no significant differences in the Bishop Score change, caesarean

delivery rate, and the incidence of tachysystole, hypersystole and hyperstimulation. They concluded that intravaginal Misoprostol is more effective than intravaginal Dinoprostone for labour induction.

Stitely M. L. et al. 1999 observed that vaginal Misoprostol is effective for outpatient cervical ripening. Out of 60 patients ; 27 (45 %) received Misoprostol and 33 (55 %) received plecebo. The majority 24 of 27 (88.9 %) of study group patients entered in active labour within 48 hours after dosing, compared with 16 % (5 of 33) of placebo group patients. The time from initial dose to delivery was significantly shorter in Misoprostol group (36.9 $\pm$ 3.8 hours compared with 61.3 $\pm$ 3.8 hours $p < 0.001$)

Belfrage P. et al (2000) compared vaginal Misoprostol with intra cervical Dinoprostone for cervical ripening and induction of labour. Of 210 women randomly assigned to receive either 50 microgram Misoprostol vaginally 6 hourly upto 4 doses or 0.5 milligram Dinoprostone gel intra cervically every 12 hours for a maximum of 2 doses. All those treated with Misoprostol gained a ripe cervix within 24 hours, whereas 8 of the 90 patients treated with Dinoprostone had no improvement in cervical ripening. For the group treated with Misoprostol, the mean induction to delivery time was significantly less and fewer patients required treatment with oxytocin. In primigravida induction-delivery interval was 16.7 hours in Misoprostol group compared to 20.4 hours in Dinoprostone ($p < 0.05$). In multigravida induction-delivery interval was 12.1 hours in Misoprostol group as compared to 15.9 hours in Dinoprostone group ($p < 0.05$). However caesarean deliveries for suspected fetal asphyxia were more in misoprostol group. They suggested that misoprostol is more efficacious, cost effective and convenient than dinoprostone for induction of labour.

Charoenkul S. et al (2000) compared the efficacy and safety of single dose of 50 microgram Misoprostol vaginally to single dose of 3 milligram Dinoprostone vaginally for pre induction cervical ripening in one hundred and forty three term pregnant women. The change in Bishop score after 24 hours of medication was one unit higher in Misoprostol treated patients compared to Dinoprostone (6.5 verses 5.5, p=0.042). No significant difference was found regarding number of vaginal deliveries within 24 hours (46.3 % verses 35.7 %, p=>0.350) and neonatal outcome in both groups. But there was a higher frequency of hyperstimulation syndrome in Misoprostol group.

Day L. (2000) compared the outcomes of 177 pregnant women induced with dinoprostone with 243 women whose labour were induced with misoprostol. They demonstrated a significant reduction in induction delivery interval and oxytocin augmentation in misoprostol group compared to dinoprostone group. There was no significant difference in mode of delivery and neonatal outcome in both groups. There was a significantly increased rate of tachysystole in the misoprostol group but not of hyperstimulation. There was no untoward maternal or fetal event. They pointed out that failed induction was uncommon where misoprostol was used and there are considerable cost savings involved in using this more effective labour induction agent.

Fernandez E and Vavilala S. (2000) evaluated the effect of Misoprostol in 200 women requiring induction of labour. 50 microgram of Misoprostol was given vaginally every four hours until a maximum of 6 doses. They observed that most of the patients delivered vaginally within 24 hours and the average induction delivery interval was 10.34$\pm$1.14 hours. They concluded that vaginal Misoprostol for induction of labour appears to be an effective method. They stated - This powerful

little tablet can work wonders and save time, energy and money for many - but this should be used with caution and respect".

Gunalap. and Bildirci I (2000) evaluated the effect of vaginal pH on the efficacy of Misoprostol for induction of labour 2 groups were generated, 68 women with a vaginal pH < 5 and 38 with vaginal pH > 5. All women received Misoprostol tablet 50 microgram every four hours upto 3 doses vaginally. The average induction-delivery interval was shorter and oxytocin augmentation was require lower pH group, but no significant difference in-caesarean section, rates or adverse maternal or foetal outcome was noted. The extent of absorption of misoprostol was reported to be highly variable among individuals. This may be explained by the altered dissolution of the tablet along with the absorption kinetics of the agent in the presence of lower PH.

Katz VL et al, (2000) evaluated use of Misoprostol for cervical ripening and induction of labour. Total of 470 patients were induced; 254 with Misoprostol and 144 with Dinoprostone. With Misoprostol, the mean time from beginning of contractions until delivery was 7 hours, 30 minutes. Vaginal birth occured in 85% of cases and spontaneous labour occured in 38%. Hyperstimulation occured in 1.6% and precipitate labour in 3%. All infants were discharged in excellent conditon. 1 baby had 5 minutes Apgar 7, and 33 (13%) had meconium, none with aspiration. 23 pateints with previous Caesarian section got Misoprostol and delivered vaginally.

Lee HY in 2000 conducted -a randomised study to compare vaginal Misoprostol Vs dinoprostone for cervical ripening and labour induction in prolonged pregnancy. 50 patients with prolonged pregnancy were treated with two hundred microgram of intravaginal Misoprostol and compared

with equal number of patients treated with 3 mg of dinoprostone. In the Misoprostol group, labour was successfully established in 92% of cases compared to 64% in the dinoprostone group (P=0.04). The induction delivery interval was shorter with more women delivering within 12 hours (72% Vs 28% P=0.047). Maternal and neonatal complications, mode of delivery, the need for oxytocin were quite similar statistically. Polysystole was more frequent (28% Vs 12% P=0.28) in the Misoprostol group, but it was not associated with fetal distress. They concluded that Misoprostol was a more effective drug for labour induction.

Ramsey PS et al, (2000) evaluated the effects of vaginal pH on efficacy of Misoprostol for cervical ripening and labour induction. Thirty seven gravid women with unfavourable cervix and indication for labour induction were enrolled in this prospective, double blind, study. All patients received 50 microgram Misoprostol intravaginaly every 6 hours for 12 hours. Average initial vaginal pH was 4.8 $\pm$ 0.5 (range, 3.5 - 7.0) for the study cohort. No significant differences were noted between those patients with low vaginal pH ($<$ 4.5) compared with those with high pH ($>$ 4.5) with respect to maternal age, parity, gestational age or initial Bishop score. The analysis revealed no significant association between vaginal pH and Bishop score change during preinduction interval, time to active labour, time to complete dilatation or time to delivery. Thus, vaginal pH does not seems to influence the efficacy of intravaginal Misoprostol.

Surekha R, et al (2000) did descriptive study to assess the effect of single dose of 50 microgram Misoprostol vaginally for induction of labour in 86 patients. 62 (72 %) of the 86 patients in the study entered active labour. There was a marked improvement in the Bishop's score among multiparas as compared to nulliparas (7.4 $\pm$ 3 verses 5.9 $\pm$ 2.9). 60 (69.7 %) delivered vaginally within 24 hours. 83 % of the vaginal

deliveries occurred within 12 hours of application of the drug. Tachysystol was the most common side effects which was observed in 8 (9.3 %) patients. Meconium staining of liquor occurred in 13.6 % of patients and three neonates developed Meconium aspiration syndrome. Mean induction to delivery interval was 9.09 $\pm$ 4 hours. They concluded that the drug may be used safely for induction of labour but the safety margin appeared to be dose dependant.

Wilk M. et al, (2000) tested the effectiveness of Misoprostol in induction of labour in prolonged pregnancies. 50 pregnant women with prolonged pregnancy, cephalic presentation, longitudinal foetus lie, existing foetal membranes and lack of spontaneous delivery action were given intravaginal 50 microgram of Misoprostol. Effectiveness of inducing, delivery lasting, labour termination and infant condition at birth were noted. Result were matched with control group of 35 patients with physiological pregnancy, who delivered in spontaneous partus. Effective provocation was observed in 38 patients, natural delivery in 40 patients. In 10 cases caesarean section was done. Lasting time of birth, way of finishing, infant condition at birth and number of complications do not statistically differ between the two groups. The study concluded that Misoprostol is an effective and safe method in induction of prolonged pregnancy.

Abdel-Aleem H et al (2001) did prospective study to explore the use of rectal Misoprostol in treatment of severe cases of atonic postpartum hemorrhage not responding to oxytocin, methyl Ergometrine and prostaglandin $F_{2\alpha}$ Among the 18 cases, 16 cases-responded promptly to Misoprostol (88.2_%). The effect appeared within 30 seconds to 3 minutes (mean = 1.4 minutes).

Carlan S. J et al (2001) conducted a randomized study to compare oral and vaginal Misoprostol. They took 1004 women in their study of which 503 subjects were given 200 microgram oral Misoprostol and 501 subjects 50 microgram vaginal Misoprostol 6 hourly to a maximum of 6 doses. Dose was increased to 300 microgram oral and 100 microgram vaginal after 2 doses. Oral Misoprostol was associated with significantly higher frequencies of intervention (67 [13.3 %] vs. 42 [8.4%], p= 0.01), tachysystole (114 [23.6%] vs. 85 [17.6%], p=0.02) and hyperstimulation (90 [18.6%] vs. 66 [13.7 %], p=0.04) as compared to vaginal Misoprostol. There was no significant differences in caesarean rates (147 [29.2 %] vs. 120 [24 %], p=0.6), mean number of Misoprostol doses used (1.5 vs. 1.6, p=0.18) or hours from administration to delivery (24.5 vs. 25.4, p= 0.77) in both groups. No adverse neonatal outcome was noted. They concluded that oral Misoprostol had similar efficacy as vaginal Misoprostol but in association with higher frequency of excessive uterine contractility and intervention.

El - Sherbiny et al (2001) observed in their study on 185 term pregnant women that 25 microgram of Misoprostol every 4 hourly can induce labour safely and effectively. 185 women were divided into two groups , group A (93) were given 25 microgram Misoprostol and group B (92) were given 50 microgram Misoprostol every 4 hourly until the onset of labor. Abnormal uterine contraction were more common in group B compared to group A. 33 (35.86 %) Vs. 10 (10.75 %) cases. The induction delivery interval was significantly shorter in group B (17.18 $\pm$ 8.48 hours in group A and 9.37 $\pm$ 5.87 hrs in group B) ($p < 0.05$). The caesarean rate was 17.20% in group A and 14.13% in group B. Postpartum hemorrhage occurred in 9.78 % of women in group B compared to 2.15% in group A.

Ghidini A. et al 2001 compared safety and efficacy of Misoprostol in different doses regimens (i.e. 50 microgram and 100 microgram) for induction of labour at term. In 58 women who were randomised to receive either 100 microgram of Misoprostol (n=26) or 50 microgram (n=32). Both group had similar mean Bishop's Score at induction (4.0 $\pm$ 2.3 hours vs. 4.1 $\pm$ 2.2 hours). The mean induction-delivery interval (hours) (11.9 $\pm$ 7.3 hours vs. 14.3 $\pm$ 9.6 hours) and caesarean section rate (35 % vs. 19 %) was not different in 100 Vs. 50 microgram groups. The rates of uterine hyperstimulation and meconium passage are found to be significantly /higher in women receiving vaginal misoprostol at doses > 25 microgram compared with conventional methods of cervical ripening and labour induction. The dose of 25 microgram misoprostol appears to be a prudent choice. Such dose is currently recommended by the American College of Obstetricians and Gynecologists.

Hofmeyr GJ & Gulmezoglu (2001) determined the effects of vaginal misoprostol for third trimester cervical ripening and induction of labour. 45 trials comparing vaginal misoprostol with placebo / no treatment or other methods of labour induction (Prostaglandin E_2 & Oxytocin) were included. Compared to placebo, misoprostol was associated with increased cervical ripening after 12 to 24 hours, reduced need for oxytocin augmentation and reduced failure rate to achieve vaginal delivery within 24 hours.

Compared to vaginal prostaglandin E_2, intracervical prostaglandin E_2 and oxytocin, vaginal misoprostol resulted in fewer failures to achieve vaginal delivery within 24 hours but was associated with more uterine hyperstimulation without fetal heart rate change.

Compared to oxytocin induction, caesarean section rate and epidural analgesia was reduced with misoprostol. Lower doses of misoprostol compared to high doses did not show significant differences except for more need for oxytocin augmentation and less uterine hyperstimulation, with and without fetal heart rate changes in low dose group. Reviewer's conclusion was that although vaginal misoprostol appeared to be more effective than conventional methods of cervical ripening and labour induction, the apparent increase in uterine hyperstimulation was of concern.

The objective of Hoftneyr G.J. Matonhodza et al (2001) was to develop a new method of misoprostol use for labour induction, using very small frequent titrated oral dosages and to demonstrate its effectiveness. The study of this method was undertaken in 25 pregnant women with various indications for induction of labour. 20 microgram misoprostol tablet was given orally 2 hourly. The dose was increased to 40 microgram after three doses. To administer such small doses one misoprostol tablet (200 μg) was dissolved in 200ml water. Eighteen (72%) women delivered vaginally within 32 hours of induction and two women developed uterine hyperstimulation. The caesarean section rate was 20%. The conclusion was that women may respond to much smaller dosages of misoprostol than are currently in use.

Hoffman R.A.M., et al (2001) evaluated the efficacy of oral Misoprostol for induction of labour in 88 women with prelabour rupture of membrane at term. 47 patients were given 100 microgram Misoprostol orally and 49 patients in the placebo group received two doses of vitamin after 6 hour interval. Median induction to delivery interval in Misoprostol group was 7.5 hours and 25 hours in the placebo group ($p < 0.001$). No significant differences were observed in the incidence of abnormalities on

the cardiotocograph, mode of delivery and neonatal outcome. They pointed out that oral Misoprostol is an effective and cheap alternative for induction of labour in patients with prelabour rupture of membrane. A problem with misoprostol, as with other oxytocics is that its action can not be predicted. Precipitate labour may occur particularly in parous patients so a lower dose might be preferable for these women.

How H.Y. et al (2001) compared the efficacy of different routes of Misoprostol administration for cervical ripening and the induction of labour 330 women at > 32 weeks gestation with a Bishop score < 6 were divided in 3 groups :

Group I - 25 microgram Misoprostol orally plus 25 microgram Misoprostol vaginally. Group II - Placebo orally plus 25 microgram Misoprostol vaginally or, Group III 25 microgram Misoprostol orally plus Placebo vaginally.

Doses were repeated every 4 hours until onset of labour or a maximum of 12 doses. The percentage of women who achieved delivery within 24 hours was highest in vaginally administered Misoprostol group : 67 % compared with 53 % in oral plus vaginal group ($p < 0.05$) and 36 % in oral group ($p < 0.05$). The median time to vaginal delivery was shorter in the vaginal and oral plus vaginal Misoprostol groups, 13.5 hours and 14.3 hours respectively when compared with 23.9 hours in the oral group ($p < 0.05$). The rate of caesarean delivery was lowest in the vaginal Misoprostol group (17%) compared with 30 % in the "oral plus vaginal" group and 32 % in the oral group, ($p < 0.05$). Uterine Tachysystol occurred only in 10 % of oral Misoprostol group compared with 32 % in the vaginal group and 34 % in the oral plus vaginal group ($p < 0.05$). Uterine hyperstimulation also occurred least frequently (4 %) in the oral

Misoprostol group compared with 15 % in the vaginal group and 22 % in the oral plus vaginal group, ($p < 0.05$). They concluded that vaginally administered misoprostol is more efficacious than either oral-plus-vaginal or oral-only route of administration.

Incerpi M.H. et al (2001) found that Misoprostol was no more effective than placebo for outpatient labour induction in patients with gestational diabetes. Of 120 pregnant women with diabetes mellitus, 57 women received 25 microgram Misoprostol and 63 received placebo vaginally on day 1 and 4 of a 7 day outpatient cervical ripening period. Similar numbers of Misoprostol and Placebo treated women delivered within 7 days of the first dose (54 % vs. 57 %, $p= 0.63$) and the mean interval from induction to delivery was similar (8530.5 minutes $\pm$ 1439.7 minutes verses 6712.5 minutes $\pm$ 606.4 minutes, $p=0.23$).

Kwon JS, (2001), compared the efficacy of oral with vaginal Misoprostol for induction of labour at term. One hundred and sixty seven women requiring induction of labour were randomised to receive 50 microgram of Misoprostol orally or vaginally every 6 hourly until the cervix was favourable or active labour occurred. The mean induction to delivery time was significantly shorter with vaginal Misoprostol compared with oral Misoprostol (15 hours Vs 23.0 hours, $P= 0.0013$). There was no difference between the two routes of administration with respect to rates of hyperstimulation or neonatal asphyxia. There were more caesarean sections in the vaginal Misoprostol group, but the difference was not statistically significant. Compared with oral Misoprostol, vaginal Misoprostol for induction of labour at term results in a shorter induction to delivery time, with fewer doses required per patient.

Leszczynska et al (2001) did a comparative analysis of effectiveness and safety of misoprostol and PGE_2 in cervical ripening and labour induction in patients with term pregnancy with a live fetus and indication for inducing labour due to an unripe cervix. Out of total 56 patients, 30 patients received misoprostol vaginally (group M) and 26 patients were induced with PGEs (group P). Time from administration of drug to onset of regular uterine contraction and induction delivery interval was shorter in group of patients receiving misoprostol compared to PGE2 group. They indicated that misoprostol is an effective drug that can be used for elective preinduction ripening and induction of labour but require special caution and care to assure safety of both the mother and the infant.

Palak et al (2001) compared labour induction intervals between vaginal misoprostol and intravenous oxytocin as well as side effects of induction in one hundred women with post term pregnancies with intact membranes. These women were given either 50 microgram vaginal misoprostol every 12 hours as needed to maximum 150 microgram or induced with intravenous oxytocin. The mean time to vaginal delivery in misoprostol group was 20.6 ± 15.2 hours compared to 11.23 ± 7.4 hours in oxytocin group ($p = 0.0396$). In misoprostol group induction failed in only 12 % cases whereas in oxytocin group in 32% cases. Episodes of vomiting were more frequent in misoprostol treated group compared to oxytocin group (22% vs 6%). They concluded that oxytocin stimulation resulted in a shorter induction delivery interval but failed induction was lesser in misoprostol group.

Sahin et al (2001) compared the efficacy and complication of vaginal misoprostol for induction of labour in 101 patients at term with and without toxemia of pregnancy. Forty two patients with toxemia of pregnancy (group I) and 59 women without toxemia (group II) with

Bishop score < 6 were induced with 50 pg misoprostol vaginally 4 hourly (maximum 4 doses).

The rates of vaginal delivery were 73.8 % and 84.6 %, need for oxytocin augmentation were 4.8 % and 5.1 % and mean insertion to delivery times were 12.5 hours and 13.8 hours in group I and II respectively. No significant difference was noticed regarding neonatal outcome, uterine contraction abnormalities and gastrointestinal side effects in both groups. They reported that vaginal misoprostol is an equally effective and safe method of labour induction in patients with toxemia of pregnancy and in normal pregnant women.

Shetty A et al, (2001), compared the efficacy of oral and vaginal doses of Misoprostol in labour induction of patients at term. Two hundred and forty five pregnant women at term, with medical or obstetrical indications for labour induction and unfavourable cervices were randomly assigned to receive 50 microgram of Misoprostol orally or vaginally. The mean interval from induction to vaginal delivery, was significantly shorter in the vaginal group compared with the oral group (17.8 h Vs 27.9 h). More women delivered within 24 hours in vaginal group (80%) as compared to oral group (46.3%). There was no difference in mode of delivery or neonatal outcomes in the two groups. There was higher incidence of uterine hyperstimutation in the vaginal group (4.9% Vs 0.8%) and more caesarean sections were performed for foetal distress in this group (13% Vs 2.4%). Although, the overall operative delivery rate was similar in the two groups. They concluded that, Misoprostol effectively induces labour, with the vaginal route of administration having a faster action than the oral route in equivalent doses. However, the more frequent occurrence of hyperstimulation and the higher intervention rate for foetal

distress in the vaginal group could mean that the preferred route might be oral.

Sanchez-Ramos et al (2002) systematically reviewed the published randomized controlled trials, to compare the safety and efficacy of 25 microgram versus 50microgram of intravaginal misoprostol for cervical ripening and labour induction. In meta-analysis of five randomized controlled trials tachysystole and hyperstimulation syndrome occurred less frequently among women who received 25 microgram misoprostol than 50 microgram. However neonatal outcome was comparable in both regimen.

Regarding efficacy, use of the 50 microgram dose was associated with a shorter vaginal delivery, greater proportion of deliveries within 24 hours, and less frequent need for oxytocin augmentation. They reported that published data indicate that intravaginal misoprostol at doses of 50 microgram for cervical ripening and labour induction is more efficacious but it is unclear whether it is as safe as the 25 microgram dose.

Shatty et al (2002) conducted a comparative trial to evaluate efficacy and patient acceptability of 50 microgram_sublingual misoprostol with 100 microgram oral misoprostol in induction of labour in 250 women at term. In both groups, dose was repeated every 4 hourly, to a maximum of five doses. There was no significant difference in the number of women delivered vaginally with in 24 hours of the induction in the sublingual group as compared with oral group (62.8% vs 59%), or in the mean induction to delivery time (21.8 hours vs 24.1 hours). There was no difference in the uterine hyperstimulation rates (1.6 % in both groups), operative delivery or neonatal outcomes. In the sublingual group, 92.6% women found the induction acceptable with 15.8 % finding tablets with an unpleasant taste, while oral route it was acceptable to 96.9% women and

4% women find it unpleasant. The conclusion was that 50 microgram sublingual misoprostol every 4 hourly has same efficacy and safety profile as 100 microgram misoprostol orally, but the oral route might be preferred by women.

Wing et at (2002) determined whether maternal age, height, weight, parity, duration of pregnancy, cervical dilatation or Bishop Score, and birth weight could be used to predict the likelihood of successful induction in the pregnant women given intravaginal misoprostol. A computerized database was complied of 1373 pregnancies with Bishop Score < 4 in which intravaginal misoprostol was given in the dose of 25 to 50 microgram 3 to 6 hourly. 675 pregnant women (48%) had successful induction. Parity (OR 2.4, 95% Cl 2.0-3.0, p< 0.001), initial cervical dilatation (OR 1.7, 95% CI 1.4-2.1, p< 0.001) and estimated gestation age (OR 1.3, 95% Cl 1.1-1.6, p = 0.003) were significant independent predictors of successful induction, but initial Bishop Score was not significant (p = 0.19).

Material and Methods

MATERIAL AND METHODS

The present study was a comparative study conducted on 252 pregnant women of age group between 18-35 years with singleton pregnancy of 36 to 42 weeks, cephalic presentation with no contraindication to vaginal delivery and with no history of previous caesarean delivery or any uterine scar. The study group was divided in 3 groups, 80 pregnant women were given 25 microgram Misoprostol vaginally 3 hourly (Group I), while 80 pregnant women were given 50 microgram Misoprostol vaginally 6 hourly (Group II). Maximum total dose used in both groups was 200 microgram. 100 pregnant women were induced with intravenous oxytocin infusion (Group III).

All study inductions were carried out on an inpatient basis admitted in Maharani Laxmi Bai Medical College, Jhansi Department of Obstetrics and Gynecology, over a 12 month period from August 2003 to August 2004.

A detailed history was elicited with special reference to obstetric history of present and past pregnancies, duration of gestation and any associated complaints. Patients were inquired about their age, gravidity, parity, socio-economic status and education, dietary and personal habits. Past history regarding any medical illness as chronic hypertension, diabetes was taken.

Socio-economic status was assessed according to Kuppu Swamy's classification (1962) based in education, occupation and income.

A general examination was performed and this was followed by examination of cardiovascular, respiratory and nervous system. The

baseline pulse rate, blood pressure, temperature and respiratory rate were recorded.

Per abdominal examination was done to note the fundal height, foetal lie, presentation, position of presenting part and duration and intensity of uterine contractions were observed for at least 10 minutes. Foetal heart sound was noted for rate, rhythm and regularity.

A perspeculum examination was done to note any discharge or leaking per vaginum then pervaginal examination was done to note the Bishop score (Consistency, position, dilatation and effcement of cervix, station of head), status of membranes and pelvic assessment.

Bishop's pre induction cervical scoring system

Factors	Score			
	0	1	2	3
Cervix				
Dilatation (cm)	Closed	1-2	3-4	5+
Effacement (%)	0-30	40-50	60-70	80+
Consistency	firm	medium	soft	
Position	Posterior	Midline	Anterior	
Head Station	-3	-2	-1,0	+1, +2
Total Score = 13, Favourable Score = 6 -13, Unfavourable Score = 0-5				

The following baseline investigations were carried out.

- Blood group and Rh typing
- Haemoglobin percentage.

• Complete urine examination - Routine & Microscopic

When necessary other investigation like blood urea, serum creatinine, serum bilirubin, USG was done.

Inclusion Criteria

The study and the control group included 260 pregnant women of

- Age Group between 18-35 years
- 36-42 weeks gestation
- Singleton pregnancy
- Uncomplicated primigravida and multigravida
- Cephalic presentation
- No contraindication to vaginal delivery
- Cervical dilation < 3 cm
- Fewer than 12 contractions per hour
- Women in whom labour induction was indicated for one or more of the following medical/obstetric reason.

  - Pregnancy induced hypertension (PIH).
  - Premature rupture of membrane (PROM).
  - Diabetes mellitus.
  - Chronic hypertension.
  - Congenital foetal anamolies.
  - Rh isoimmunization.
  - Intra uterine foetal death.
  - Intra uterine growth restriction. (IUGR).

Exclusion Criteria:-

Following cases were excluded from this study.

- Cepahlo-pelvic disproportion.
- Malpresentation.

- History of epilepsy, glaucoma, sickle cell disease or patients having known hypersensitivity to prostaglandins.
- Antepartum haemorrhage
- Pre existing foetal distress.
- Grand multipara.
- Medical disorders like heart disease, chronic renal failure.
- Previous uterine scar like caesarean, myomectomy.
- History of previous difficult or traumatic labour.

The cases were divided into 3 groups :

- Group I - Those who received 25 microgram misoprostol tablet 3 hourly vaginally
- Group II - Those who received 50 microgram misoprostol tablet 6 hourly vaginally
- Group III - Cases induced with intravenous oxytocin infusion

STUDY GROUP		
Cases were divided in 3 groups		
Group	No. of Patients	Method of Induction
Group I	80	25 Microgram 3 hourly vaginally. Maximum total dose 200 microgram
Group II	80	50 Microgram 6 hourly vaginally. Maximum total dose 200 microgram
Group III	100	Intravenous Oxytocin infusion

Procedure

Patient was laid down in dorsal position. Bishop scoring was done. The Misoprostol tablet was divided in either 25 microgram dose (1/4th of

100 microgram tablet) or 50 microgram dose (1/2 of 100 microgram tablet). The drug was inserted in posterior fornix of vagina taking aseptic precautions. The dose used was either 25 microgram 3 hourly or 50 microgram 6 hourly. Time of insertion of drug was noted in each case. The patient was kept in the recumbent position for half an hour after insertion of the tablet. Maximum total dose used was 200 microgram. Labour was monitored including vital signs, time of onset and duration of uterine contractions and foetal heart rate was noted.

Per vaginal examination was repeated before next dose and as an when required to note the progress of labour. The dose was repeated until labour was established or upto maximum of 200 microgram drug used.

- A half hourly monitoring of pulse rate, blood pressure, temperature, hydration, foetal heart rate, uterine contractions was done.
- A 4 hourly vaginal examination was done to assess cervical dilatation, effacement, descent of head, presence of membranes, colour of liquor and moulding if membranes were absent.
- Vaginal delivery was conducted in the usual manner and instrumental delivery (forceps) was performed when indicated.
- All cases were observed for 1 hour after delivery in the 4th stage of labour for any evidence of postpartum haemorrhage.

Trial interruption followed by active intervention was done whenever there was any sign of :-

1. Foetal Distress.

2. Unnoticed CPD.

3. Cervical Dystocia

4. Incoordinate Uterine Activity.

5. Maternal Exhausation.

6. Prolonged Labour.

- Induction - active labour and induction-delivery interval was noted.

- The mode of delivery was noted which could be either a vaginal delivery (including forceps) or a caesarean delivery.

- Labour complications were noted if any including abnormal uterine contractions, any irregularity in foetal heart rate, cervical tear and PPH. Any maternal side effect of drug including nausea, vomiting, diarrhea, shivering, fever were noted.

- The neonatal outcome in terms of date and time of delivery, sex, weight of baby, Apgar score at 1 min and 5 min was recorded.

- Group 1 (80 cases)-received misoprostol tablet 25 microgram vaginally 3 hourly, maximum total dose being 200 microgram (8 doses).

- Group II (80 cases) - received 50 microgram misoprostol tablet 6 hourly, maximum total dose being 200 microgram (4 doses)

- Group III (100 cases) - induced with intravenous oxytocin infusion.

Observations

OBSERVATIONS

The present study was carried out for evaluating the efficacy of vaginal misoprostol for induction of labour and to compare it with the efficacy of intravenous oxytocin infusion. The study was done on 260 pregnant women at term admitted in ***Maharani Laxmibai Medical College, Jhansi*** Department of obstetrics and Gynaecology, over a period of twelve months.

TABLE 1

DISTRIBUTION OF CASES

GROUP	NO. OF PATIENTS	METHOD OF INDUCTION
GROUP I	80	25 Microgram Misoprostol 3 hourly in posterior fornix of vagina
		Maximum total dose 200 microgram
GROUP II	80	50 Microgram Misoprostol 6 hourly in posterior fornix of vagina
		Maximum total dose 200 microgram
GROUP III	100	Intravenous Oxytocin infusion

Two hundred sixty primigravid and multigravid patients with singleton pregnancy of 36-42 weeks and cephalic presentation were selected randomly and were divided into 3 groups :

- **Group I (80 cases)** – received misoprostol 25 microgram vaginally 3 hourly, maximum total dose being 200 microgram (8 doses).
- **Group II (80 cases)** - received 50 microgram misoprostol tablet 6 hourly, maximum total dose being 200 microgram (4 doses).
- **Group III (100 cases)** – Induced with intravenous oxytocin infusion.

TABLE 2						
AGE DISTRIBUTION						
Age in Years	Group I (80)		Group II (80)		Group III (100)	
	No.	%	No.	%	No.	%
<=20	20	25.00	19	23.75	16	16.00
21 - 25	41	51.25	40	50.00	55	55.00
26 - 30	15	18.75	16	20.00	25	25.00
31 - 35	4	5.00	5	6.25	4	4.00
P Value > 0.05						

Table-2 shows that maximum cases (52.08%) in all the 3 groups were young between 21-25 years of age group All the groups were comparable regarding the age of patients, the difference was not statistically significant (P value > 0.05). (table-2).

TABLE 3						
GRAVIDITY						
GRAVIDITY	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Primigravida	41	51.25	42	52.50	54	54.00
Multigravida	39	48.75	38	47.50	46	46.00
Total	**80**	**100.00**	**80**	**100.00**	**100**	**100.00**
$\sum X^2 = 0.14$ df = 2 P Value >0.5						

In the present study both primigravidae and multigravidae having indication for induction were included. Group I comprised of 41 (51.25%) primigravidae and 39 (48.75%) multigravidae, group II included 42

(52.5%) primigravidae and 38 (47.5%) multigravidae and in group III there were 54 (54%) primigravidae and 46 (46%) multigravidae.

All the 3 groups were comparable on statistical analysis of gravidity distribution (P value > 0.5) (table-3). Grand multiparae (parity > 4) were excluded from the study.

TABLE 4

ANTENATAL CARE

The patient who had minimum 2 antenatal visits were labeled as booked cases

ANTENATAL VISIT	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
Booked	41	51.25	36	45.00	48	48.00
Unbooked	39	48.75	44	55.00	52	52.00
Total	80	100.00	80	100.00	100	100.00

P Value > 0.5

The present study shows that most of the patients were unbooked and there was no significant difference in statistical analysis.

TABLE 5						
RESIDENTIAL AREA						
RESIDENTIAL AREA	**Group I**		**Group II**		**Group III**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Urban	37	46.25	34	42.50	44	44.00
Rural	43	53.75	46	57.50	56	56.00
Total	**80**	**100.00**	**80**	**100.00**	**100**	**100.00**
P Value > 0.5						

More than half of the patients in all the 3 groups, were from urban background. All the 3 groups were comparable on the statistical analysis of residential area distribution (P value > 0.5) (table-5).

TABLE 6						
EDUCATIONAL LEVEL						
EDUCATIONAL LEVEL	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Illiterate	18	22.50	26	32.50	20	20.00
Primary	27	33.75	24	30.00	32	32.00
High School	16	20.00	14	17.50	22	20.00
Intermediate	13	16.25	10	12.50	22	22.00
University	6	7.50	6	7.50	4	4.00
$\sum X^2 = 5.34$ d.f = 8 P Value > 0.5						

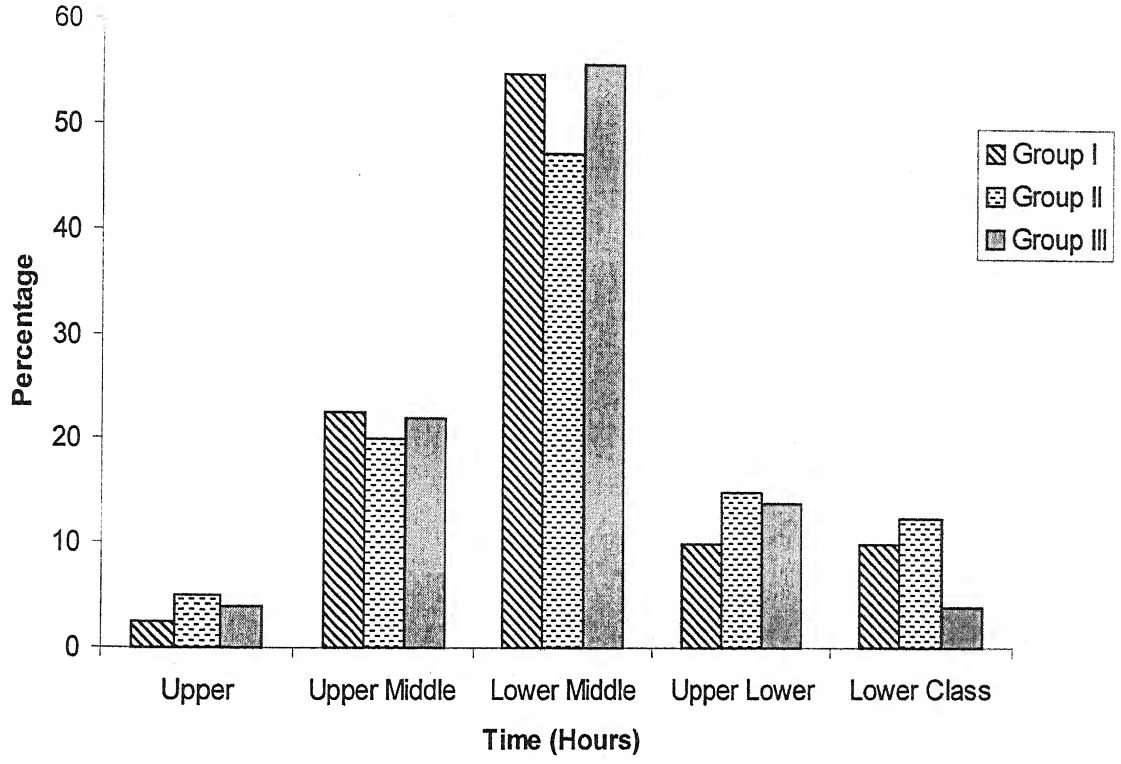
The present study shows that 50 per cent patients were illiterate in all the 3 groups. And were comparable by statistical analysis.

TABLE 7						
SOCIOECONOMIC STATUS						
SOCIAL CLASS	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Upper	2	2.50	4	5.00	4	4.00
Upper Middle	18	22.50	16	20.00	22	22.00
Lower Middle	44	55.00	38	47.50	56	56.00
Upper Lower	8	10.00	12	15.00	14	14.00
Lower Class	8	10.00	10	12.50	4	4.00
$\sum X^2 = 6.46$ d.f = 8 P Value > 0.5						

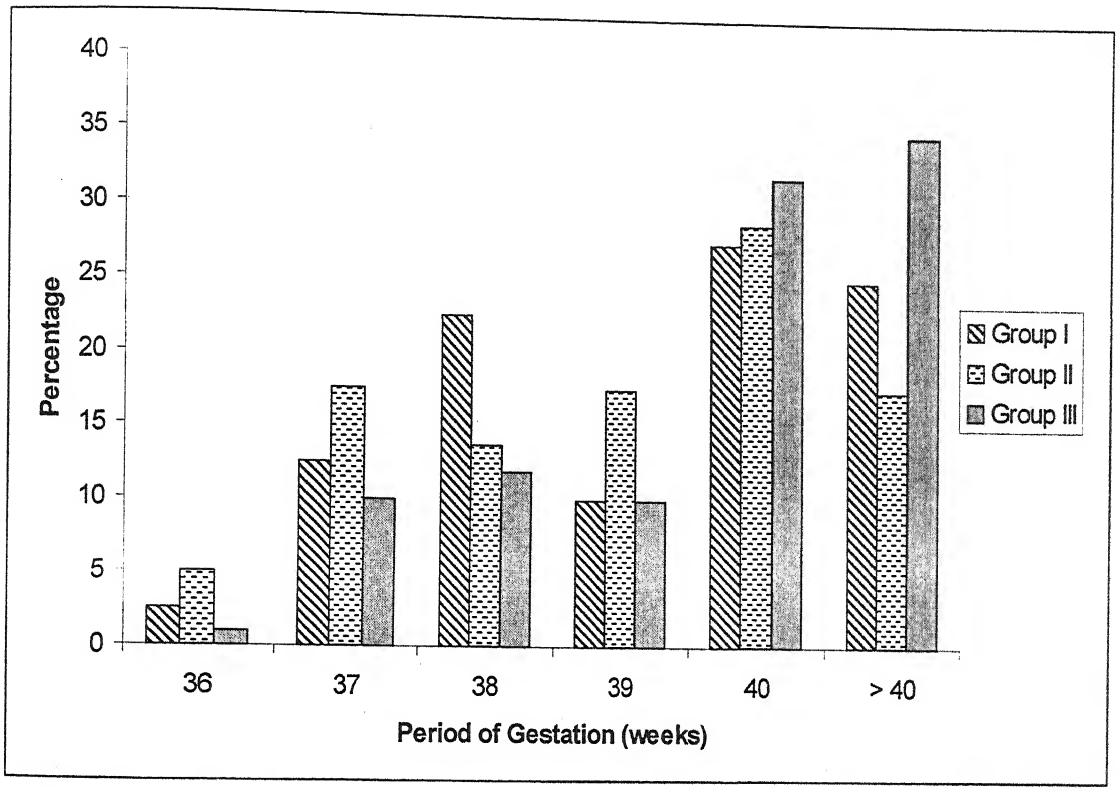
Majority of the patients i.e. 44 (55 %) in group I, 38 (47.5 %) in group II and 56 (56 %) in group III belonged to the lower middle socio-economic class.

TABLE 8						
PERIOD OF GESTATION						
GESTATIONAL AGE IN WEEKS	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
36	2	2.50	4	5.00	1	1.00
37	10	12.50	14	17.50	10	10.00
38	18	22.50	11	13.75	12	12.00
39	8	10.00	14	17.50	10	10.00
40	22	27.50	23	28.75	32	32.00
40	20	25.00	14	17.50	35	35.00
$\sum X^2 = 16.01$ d.f = 10 P Value > 0.05						

SOCIOECONOMIC STATUS



PERIOD OF GESTATION



Majority of the cases i.e. 58 (75 %) cases in group I, 62 (77.5 %) in group II and 64 (64 %) in group III belonged to 37-40 weeks of gestation. The period of gestation at which labour was induced was comparable in all the 3 groups. (P value > 0.05) (table- 8) (Fig. 1).

TABLE 9						
INDICATION FOR INDUCTION						
INDICATION	Group I (80)		Group II (80)		Group III (100)	
	No.	%	No.	%	No.	%
TERM Preg.	21	26.25	16	20.00	21	21.00
post term preg.	19	23.75	14	17.50	32	32.00
PROM	14	17.50	22	27.50	19	19.00
PIH	19	23.75	20	25.00	24	24.00
Rh-ve preg.	6	7.50	2	2.50	0	0.00
Congenital anamoly	0	0.00	3	3.75	1	1.00
IUD	1	1.25	3	3.75	3	3.00
P Value > 0.5						

The indications for induction did not differ in all the three groups with pregnancy induced hypertension (PIH), post term pregnancy and prelabour rupture of membrane (PROM) as chief causes for labour induction. As far as indication for labour induction was concerned, in all the 3 groups, the difference was not statistically significant (P value > 0.5) (Table 11) (Fig. 2)

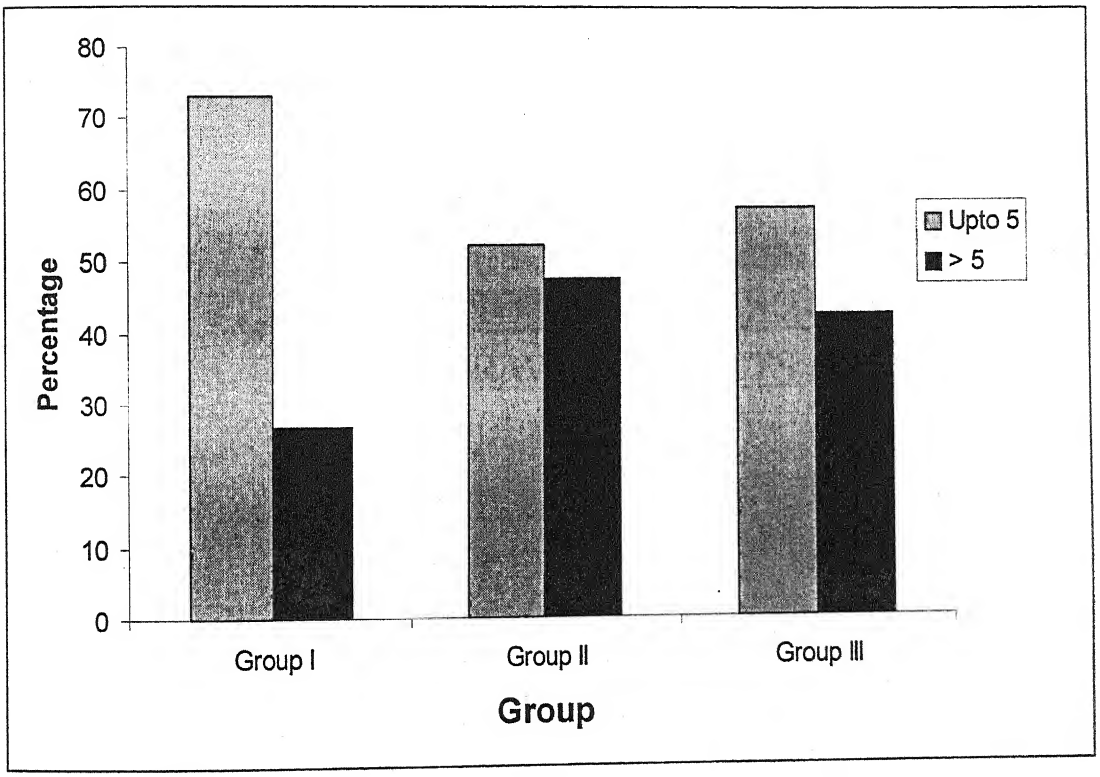
TABLE 10						
PREINDUCTION BISHOP SCORE						
Primi gravid Subjects						
BISHOP	**Group I**		**Group II**		**Group III**	
	No.	**%**	**No.**	**%**	**No.**	**%**
≤ 5	30	73.17	22	52.38	31	57.41
> 5	11	26.83	20	47.62	23	42.59
Total	41	100	42	100	54	100
$\sum X^2 = 4.13$ d.f = 2 P Value > 0.1						

In the present study, more than half (155) antenatal cases induced, were having unfavourable cervices. The difference was not significant on the basis of statistical analysis of preinduction Bishop Score in primigravidae (P< 0.1) (Table-10) (Fig. 2).

TABLE 11						
PREINDUCTION BISHOP SCORE						
Multi Gravid Subjects						
BISHOP	**Group I**		**Group II**		**Group III**	
	No.	**%**	**No.**	**%**	**No.**	**%**
≤ 5	23	58.97	24	63.16	25	54.35
> 5	16	41.03	14	36.84	21	45.65
Total	39	100	38	100	46	100
$\sum X^2 = 0.75$ d.f = 2 P Value > 0.5						

In multigravidae > 50 per cent patients have unfavorable cervices with Bishop score < 5. All the 3 groups were comparable on the basis of statistical analysis of pre-induction Bishop score in multi gravid subjects. (p value >.5)

PERINDUCTION BISHOP SCORE
PRIMI GRAVID SUBJECTS



PERINDUCTION BISHOP SCORE
MULTI GRAVID SUBJECTS

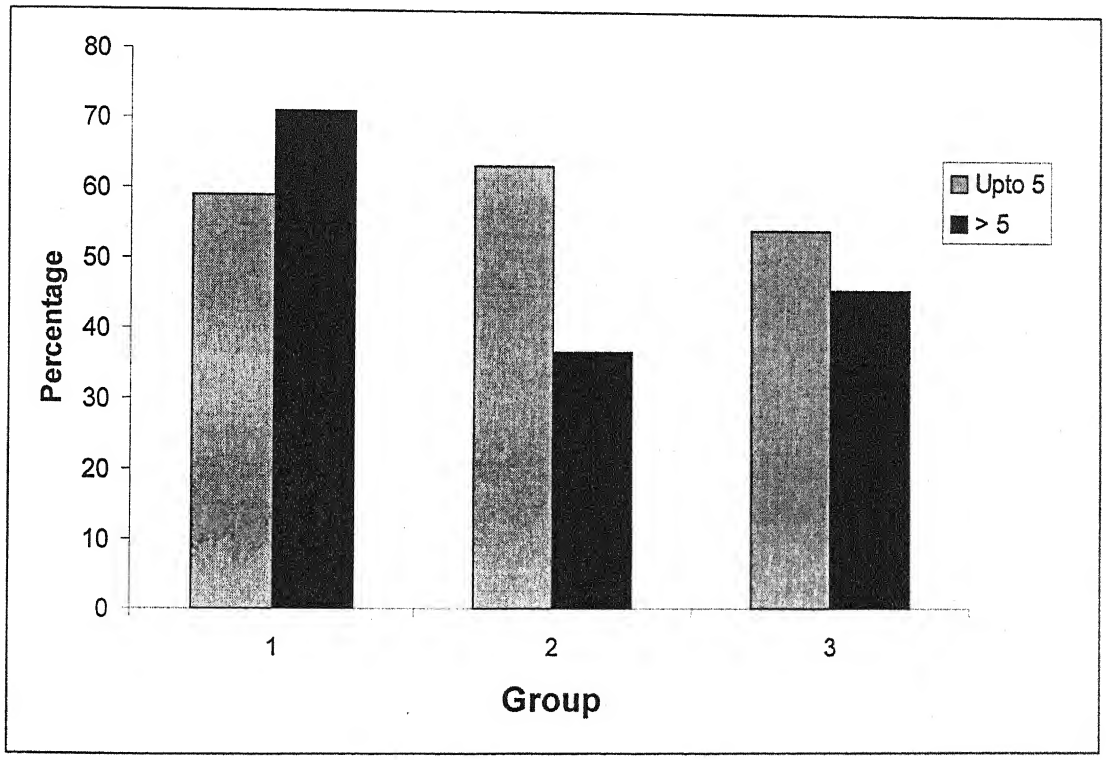


TABLE 12						
INDUCTION ACTIVE LABOUR INTERVAL						
Primi gravid Subjects						
TIME (HOURS)	**Group I (41)**		**Group II (42)**		**Group III (54)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
0 – 6	15	36.58	18	42.85	11	20.37
6 -12	20	48.78	14	33.33	12	22.22
12-18	4	9.75	7	16.66	21	38.88
18-24	2	4.87	3	7.14	10	18.51
Mean ± SD	**7.97 ± 4.76**		**8.24 ± 5.59**		**12.33 ± 6.08**	

Group	t value	p value
I VS III	3.75	<0.01
II VS III	3.31	< 0.01
I VS II	0.34	> 0.05

The mean induction active labour interval in primigravida was 7.97 ± 4.76 hours in group I 8.24 ± 5.59 hours in group II and 12.33 ± 6.08 hours in group III. On comparing the time required to reach active labour in group I and group II with that of group III was statistically significant (p value < 0.01). Where as on comparing group I and group II it was statistically insignificant. (p value > 0.05).

INDUCTION ACTIVE LABOUR INTERVAL
(PRIMI GRAVID SUBJECTS)

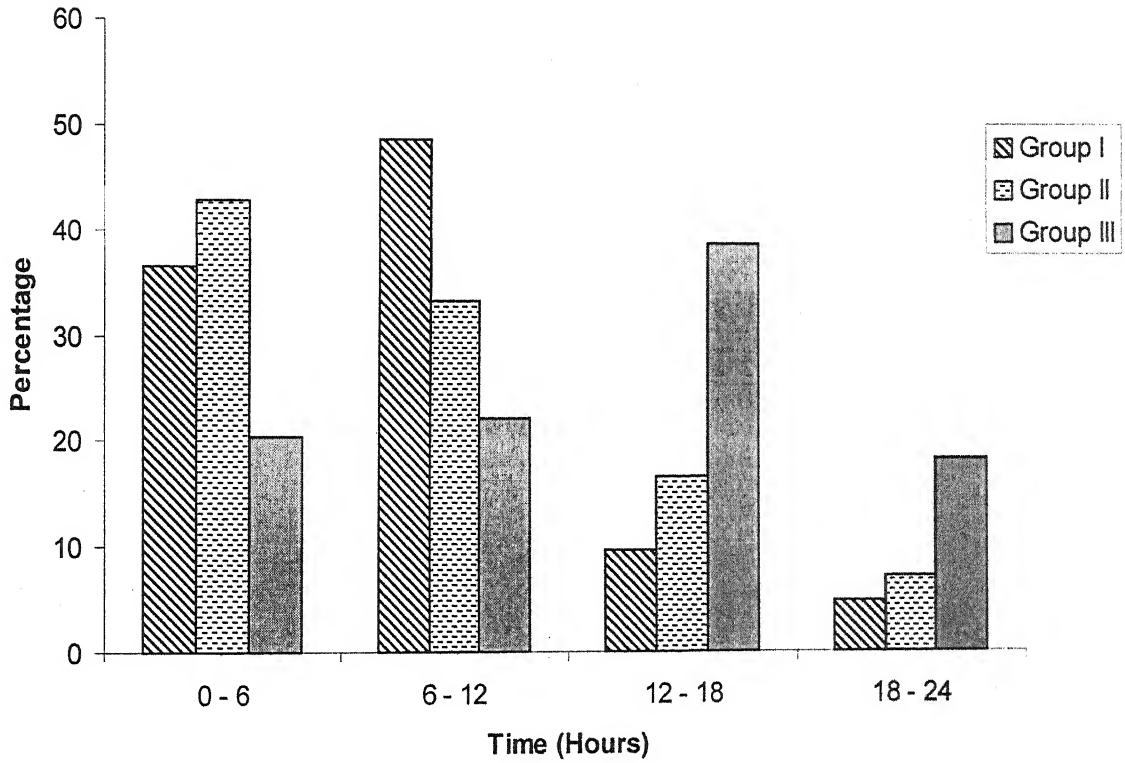


TABLE 13						
INDUCTION ACTIVE LABOUR INTERVAL						
Multi Gravid Subjects						
TIME (HOURS)	Group I (39)		Group II (38)		Group III (46)	
	No.	%	No.	%	No.	%
0 – 6	25	64.10	20	52.63	8	17.39
6 -12	12	30.76	15	39.47	10	21.73
12-18	2	5.12	3	7.89	19	41.30
18-24	0	0	0	0.00	9	19.56
Mean ± SD	5.46 ± 3.52		6.31 ± 3.82		12.78 ± 6.1	

Group	t value	p value
I VS III	6.24	<0.01
II VS III	5.59	< 0.01
I VS II	0.25	> 0.05

The mean induction active labour interval in multigravida was 546 ± 3.52 hours in group I 6.31 ± 3.82 hours in group II and 12.78 ± 6.1 hours in group III. On comparing the time required to reach active labour in group I and group II with that of group III was statistically significant (p value < 0.01). Where as on comparing group I and group II it was statistically insignificant. (p value > 0.05).

INDUCTION ACTIVE LABOUR INTERVAL
(MULTI GRAVID SUBJECTS)

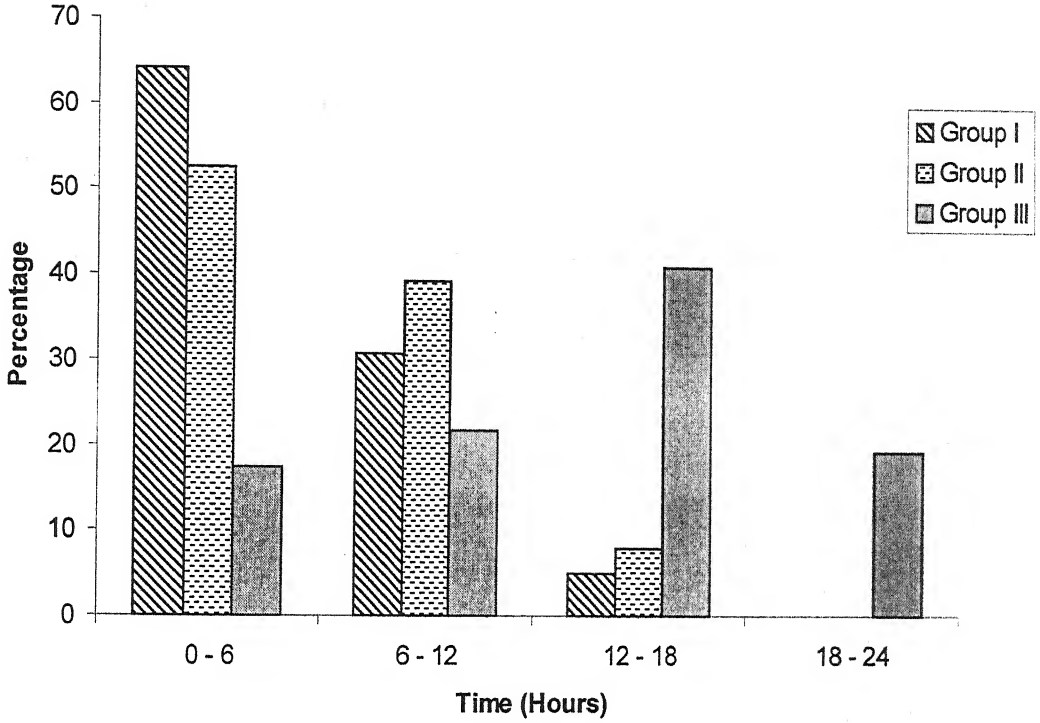


TABLE 14						
INDUCTION DELIVERY INTERVAL						
PrmiGravid Subjects						
TIME (HOURS)	**Group I (41)**		**Group II (42)**		**Group III (54)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
0 – 6	10	24.39	11	26.19	3	5.55
6 -12	20	48.78	18	42.85	8	14.81
12-18	11	26.82	13	30.95	23	42.59
18-24	0	0	0	0.00	20	37.03
Mean ± SD	**9.21 ± 4.15**		**9.28 ± 4.53**		**15.66 ± 5.14**	

Group	t value	p value
I VS III	6.15	<0.01
II VS III	6.31	< 0.01
I VS II	0.09	> 0.05

Mean induction delivery interval was 9.21 ± 4.15 hours in group I, 9.28 ± 4.53 hours in group II and 15.66 ± 5.14 hours in group III.

On comparing group I and group II with that of group III for mean induction delivery interval it was found to be statistically significant ($P<0.01$) and on comparing group I with group II it was not statistically significant ($P > 0.05$) (table - 14) (Fig. 5).

INDUCTION DELIVERY INTERVAL
(PRIMI GRAVID SUBJECTS)

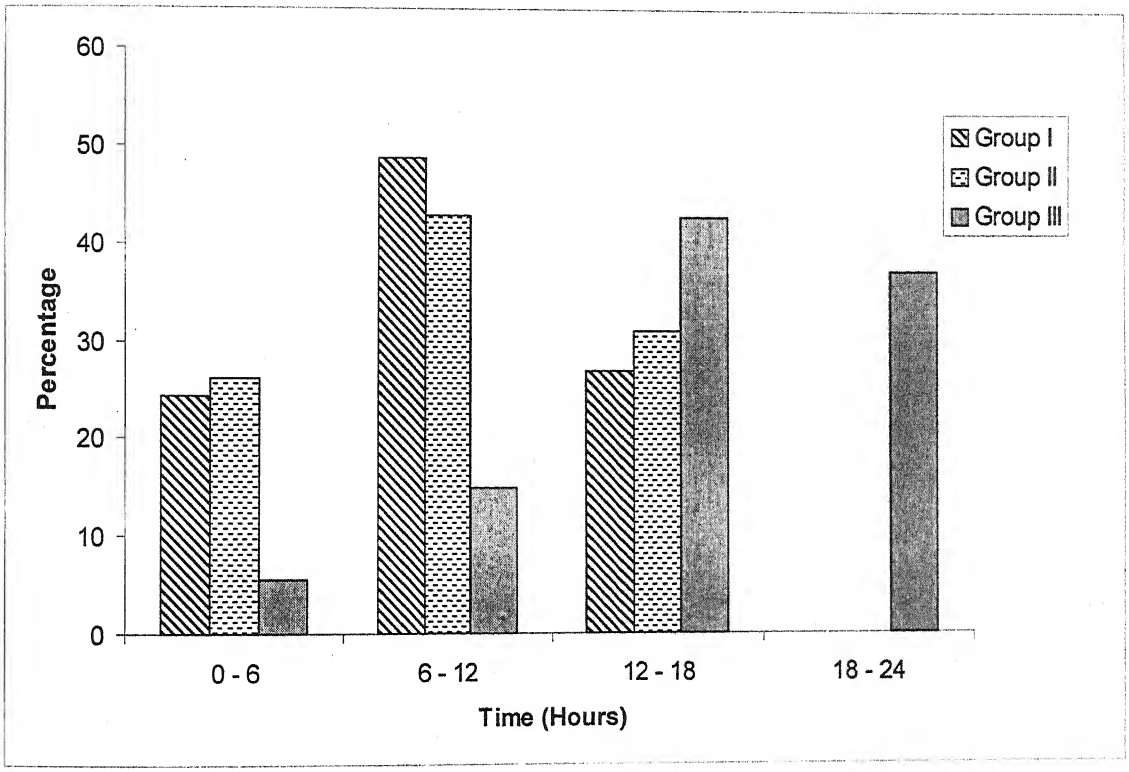


TABLE 15						
INDUCTION DELIVERY INTERVAL						
Multim Gravid Subjects						
TIME (HOURS)	Group I (41)		Group II (42)		Group III (54)	
	No.	%	No.	%	No.	%
0 – 6	20	48.78	18	47.36	4	8.69
6 -12	13	31.70	16	42.10	4	8.69
12-18	6	15.38	4	10.52	23	50.00
18-24	0	0	0	0.00	15	32.60
Mean ± SD	6.84 ± 4.41		6.78 ± 4.01		13.11 ± 7.28	

Group	t value	p value
I VS III	7.04	<0.01
II VS III	4.75	< 0.01
I VS II	0.06	> 0.05

Mean induction delivery interval was 6.84 ± 4.41 hours in group I, 6.78 ± 4.01 hours in group II and 13.11 ± 7.28 hours in group III.

On comparing group I and group II with that of group III for mean induction delivery interval it was found to be statistically significant (P<0.01) and on comparing group I with group II it was not statistically significant (P > 0.05) (table - 14) (Fig. 5).

INDUCTION DELIVERY INTERVAL
(MULTI GRAVID SUBJECTS)

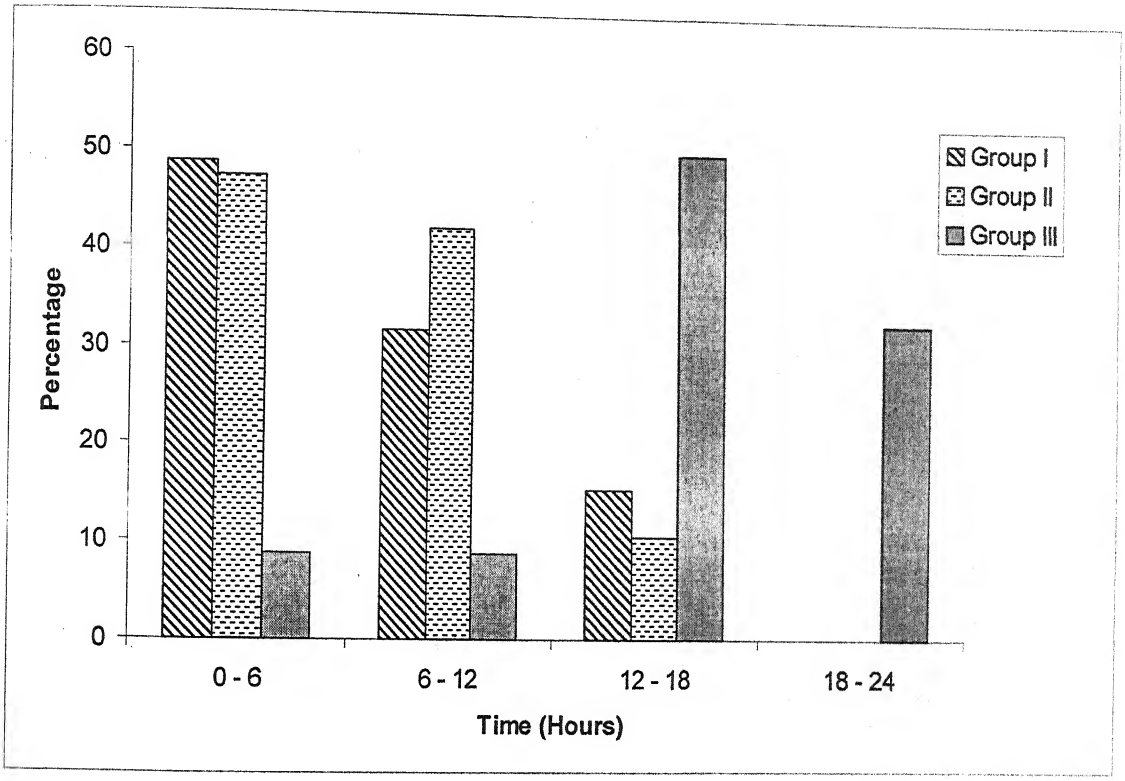


TABLE 16						
MODE OF DELIVERY						
MODE OF DELIVERY	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Spontaneous Vaginal Delivery	74	92.50	73	91.25	84	84.00
Caesarean Section	6	7.50	7	8.75	16	16.00
P > 0.05						

Majority of cases in all the 3 groups i.e. 74 (92.50 %) cases in a group I, 73 (91.25%) cases in group II and 84 (84%) cases in group III had spontaneous vaginal delivery. Caesarean section was done in 6 (7.5 %) cases in group I, 7 (8.75%) cases in group II and 16 (16 %) cases in group III. Thus regarding mode of delivery the difference was not statistically significant in all the 3 groups (P value > 0.05) (Table – 16 Fig.7.

TABLE 17						
INDICATION FOR LSCS						
INDICATIONS	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Foetal distress	2	2.50	6	7.50	8	8.00
Prolonged labour	3	3.75	1	1.25	6	6.00
Deep transverse arrest	1	1.25	0	0.00	1	1.00

In both Misoprostol and Oxytocin groups, the chief indication for caesarean section was foetal distress i.e. in 2 (2.5 %) cases in group I, 6 (7.5 %) cases in group II and 8 (8 %) cases in group III. Caesarean section

was done for prolonged first stage of labour in 3 (3.75 %) cases in group I, 1 (1.25 %) case in group II and 6 (6 %) cases in group III. Deep transverse arrest (DTA) was the indication for caesarean section in 1 (1.25 %) case in group I and 1 (1.25 %) case in group III. (Table - 17) (Fig. 8)

TABLE 18

MATERNAL COMPLICATIONS INCLUDING STAGE IV COMPLICATION

COMPLICATIONS	Group I (80)		Group II (80)		Group III (100)	
	No.	%	No.	%	No.	%
Uterine tachysystole	2	2.50	6	7.50	4	4.00
Cervical Tear	1	1.25	1	1.25	3	3.00
Postpartum Haemorrhage	2	2.50	0	0.00	4	4.00
P > 0.05						

Uterine tachysystole (>5 contractions in 10 minutes for two consecutive 10 minute period) was observed in 2 (2.5 %) cases in group I, 6 (7.5 %) cases in group II and 4 (4 %) cases in group III. Cervical tears. occurred in 1 (1.25 %) case in group I, 1 (1.25 %) case in group II and 3 (3%) cases in group III. Postpartum haemorrhage due to uterine atony was observed in 2 (2.5 %) cases in group I, and 4 (4 %) cases in group III.

There was no significant difference regarding maternal complications in all the 3 groups. Incidences of uterine tachysystole were slightly more in Group II (50 microgram group) (7.5 %) compared to group I (25 microgram) (2.5%) (Table-18) (Fig. 9).

TABLE 19						
FETAL COMPLICATIONS						
COMPLICATIONS	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Foetal Distress	2	2.50	6	7.50	9	9.00
Respiratory Distress	0	0.00	1	1.25	12	12.00
Meconium aspiration syndrome	0	0.00	0	0.00	0	0.00
Icterus	0	0.00	0	0.00	5	5.00

Foetal distress was observed in 2 (2.5 %) cases in group I, 6 (7.5 %) cases in group II and 9 (9 %) cases in group III.

There was no significant difference regarding incidence of foetal distress in both misoprostol and oxytocin group. In oxytocin group (group III) respiratory distress occurred in 12% cases and 5% neonates became icteric. (Table - 19) (Fig. 10).

TABLE 20						
APGAR SCORE AT 1 MINUTE						
APGAR SCORE	**Group I (80)**		**Group II (80)**		**Group III (100)**	
	No.	**%**	**No.**	**%**	**No.**	**%**
0 – 3	1	1.25	4	5.00	5	5.00
4 – 6	4	5.00	5	6.25	9	9.00
7 – 10	75	93.75	71	88.75	86	86.00
Mean	**7.97 ± 0.95**		**7.85 ± 1.44**		**7.65 ± 1.08**	

TABLE 21						
APGAR SCORE AT 5 MINUTE						
APGAR SCORE	Group I (80)		Group II (80)		Group III (100)	
	No.	%	No.	%	No.	%
0 – 3	1	1.25	4	5.00	5	5.00
4 – 6	0	0.00	0	0.00	0	0.00
7 – 10	79	98.75	76	95.00	95	95.00
Mean	**9.18 ± 0.66**		**9.41 ± 0.74**		**9.04 ± 1.20**	

In most of the cases in all the groups Apgar score at 1 min was 7-10 i.e. in 75 (93.75%) cases in group I 71 (88.75%) cases in group II and 86 (86%) cases in group III. Apgar Score at 1 minute was 4-6 in 4 (5%) cases in group I, 5 (6.25%) cases in group II and 9 cases in group III.

TABLE 22						
BIRTH WEIGHT						
WEIGHT (Kg)	Group I (80)		Group II (80)		Group III (100)	
	No.	%	No.	%	No.	%
> 1 – 2	4	5.00	8	10.00	6	6.00
> 2 – 3	70	87.50	64	80.00	90	90.00
> 3 – 4	6	7.50	8	10.00	4	4.00
Mean birth weight (kg)	**2.53**		**2.50**		**2.48**	

The mean birth weight was 2.53 kg. in group I, 2.50 kg. in group II and 2.48 kg. in group III (Table - 22) (Fig. 12).

TABLE 23						
MATERNAL SIDE EFFECTS						
SIDE EFFECT	Group I (80)		Group II (80)		Group III (100)	
	No.	%	No.	%	No.	%
Nausia	1	1.25	1	1.25	3	3.00
Vomitting	1	1.25	2	2.50	0	0.00
Diarrhoea	0	0.00	0	0.00	0	0.00
Fever	1	1.25	1	1.25	2	2.00

In the present study no major maternal side effect were observed. Regarding maternal side effects the difference was not significant in all the 3 groups (Table - 23) (Fig. 13).

Discussion

DISCUSSION

Many maternal and foetal conditions exist in which there is a need to terminate pregnancy before the patient goes to spontaneous Labour when the induction of Labour is necessary and the cervix is unripe, the obstetrician is faced with a management that frequently ends in caesarean delivery. A great amount of research has been directed in the last few years towards the development of effective cervical ripening agents which can induce Labour also. Induction of Labour with prostaglandin's offers the advantage of promoting cervical ripening with stimulation of myometrial Contractility. Recently misoprostol has been approved by FDA to be taken orally for the prevention and treatment of gastric ulcers associated with the use of NSAIDS. It has also become an important drug in obstetric practice because of its uterotonic and cervical ripening action.

Thus, a clinical evaluation of various methods of induction of Labour has been attempted to judge their safety & reliability. A meticulous study in search of a safe alternative for Induction of Labour has been carried out in Maharani Laxmi Bai Medical College, Jhansi.

The study was conducted on 260 pregnant women divided into three groups, group I induced with 25 μg of misoprostol intravaginaly every 3 hour & group II induced with 50 μg of misoprostol intravagninaly every 6 hours and the third group was induced with oxytocin infusion drip.

The efficacy of methods was observed. The observations were noted in terms of age, parity and period of gestation, Socio-economic status. Induction delivery interval, doses of misoprostol required, their success rate and side effects.

1) ***Relation to age :***

The study shows that maximum cases (52.08%) in all the 3 groups were young between 21-25 years of age group i.e. 41 cases (51.25 %) in group I, 40 cases (50 %) in group II and 55 cases (55 %) in group III. The youngest patient was of 18 years and the oldest was of 35 years. The age was 18-20 years in 20 (25 %) subjects in group I, 19 (23.75 %) subjects in group II and 16 (16 %) subjects in group II.I. 4 patients (5 %) in group I, 5 patients (6.25 %) in group II and 4 patients (4 %) in group III were of 31-35 year group. All the groups were comparable regarding the age of patients, the difference was not statistically significant (P value > 0.05). (table-2)

2) ***Relation to parity***

In the present study both primigravidae and multigravidae having indication for induction were included. Group I comprised of 41 (51.25%) primigravidae and 39 (48.75%) multigravidae, group II included 42 (52.5%) primigravidae and 38 (47.5%) multigravidae and in group III there were 54 (54%) primigravidae and 46 (46%) multigravidae.

All the 3 groups were comparable on statistical analysis of gravidity distribution (P value > 0.5). Grand multiparae (parity>4) were excluded from the study.

3) ***Relation to rural and urban population***

More than half of the patients in all the 3 groups, i.e. 43 (53.75%) in group I, 46 (57.5%) in group II and 56 (56%) in group III were rural dwellers. 37 (46.25%) cases in group, I 34 (42.5%) cases in group II and 44 (44%) cases in group III were from urban background. All the 3 groups

were comparable on the statistical analysis of residential area distribution (P value > 0.05).

4) *Relation to socio-economic status*

The cases were allotted social classes according to education of head of family, his occupation and per capita income per month (Kuppuswamy's classification). 18 (22.5 %) antenatal cases in group I, 16 (20 %) antenatal cases in group II and 22 (22.0%) antenatal cases in group III were of upper middle class.

In this study the majority of the patients i.e. 44 (55 %) in group I, 38 (47.5 %) in group II and 56 (56 %) in group III belonged to the lower middle socio-economic class. 16 (20 %) cases in group I, 22 (27.5 %) cases in group II and 18 (18 %) cases in group III were either of upper lower or lower socio-economic class. Minimum number of patients were of the upper class i.e. 2 (2.5 %) of group I, 4 (5 %) of group II and 4 (4 %) of group III. The difference was not significant on the basis of statistical analysis of socio-economic status. (P value > 0.5).

5) *Relation to period of gestation*

All the women were grouped as per the duration of pregnancy in weeks. Period of gestation was 36 weeks in 2 (2.5 %) cases in group I, 4 (5 %) cases in group II and 1 case in group III. Majority of the cases i.e. 58 (75 %) cases in group I, 62 (77.5 %) in group II and 64 (64 %) in group III belonged to 37-40 weeks of gestation. Period of gestation was > 40 weeks in 20 (25 %) cases in group I, 14 (17.5 %) cases in group II and 35 (35 %) cases in group III . The period of gestation at which labour was induced was comparable in all the 3 groups. (P value > 0.05).

6) *Relation of induction delivery interval*

The present study shows that induction delivery interval is remarkably shortened in women induced with misoprostol compared to those induced with Oxytocin.

In primigravidae maximum number of women induced with misoprostol i.e. 20 (48.78%) in group I, 18 (42.85%) in group II, delivered in 6-12 hours duration while only 8 (14.81%) primigravidae in Oxytocin group delivered within 6-12 hours of induction.

Induction delivery interval was 12-18 hours in 11 (26.83%) primigravidae in group I and in similar number of cases in group II.

Most primigravidae in group III i.e. 23 (42.59%) delivered in 12-18 hours duration. 20 (37.03%) primigravid patients in oxytocin group (Group III) delivered in 18-24 hours of induction.

In multigravidae, 20 (48.78%) patients in group I, 18 (47.36%) patients in group II and 4 (8.69%) patients in group III delivered in 6 hours of induction.

Induction delivery interval was 6-12 hours in 13 (31.70%) multigravid patients in group I, 16 (42.10%) multigravid patients in group II and 4 (8.69%) multigravid subjects in group III. Greater than 12-18 hours were required to deliver in 23 (50.0%) multigravid subjects in oxytocin group (group III) while only 6 (15.38%) multigravidae in group I and 4 (10.53%) multigravidae in group III required 18-24 hours to deliver.

15 (32.60%) multigravidae in group III required 18-24 hours to deliver.

The mean Induction delivery interval by misoprostol administration vaginally as reported by different authors in different studies is :-

1) Margulies et al (1992) reported induction delivery intervel was 407 ± 265 min in misoprostol group (dose 50 μg vaginally) and 577 ± 605 in oxytocin group.

2) Pletcher et al (1993) conducted a double blind trial to determine the effectiveness of Intravaginal misoprostol in improving bishop score, leading to an early safe vaginal delivery, the change in bishop score was 5.3 in misoprostol group compared to 1.5 in placebo group. The mean time from insertion to delivery was 15.6 h in the former which it was 43.2 h in the placebo group.

3) Sanchez - Ramoz, Kaunitz et al (1993) reported induction delivery interval was 11 hours in misoprostol group and 8 hours in oxytocin group.

4) Bugalho A, Bique C, Bergstrom S (1995)

Reported that the Induction to delivery intervals in the oxytocin and misoprostol (50 - 100 μg) groups, respectively, had the following duration with Bishop score < 6, 24.3 VS 14.4 hours (P = 0.002), with Bishop's score more than or 6, 10.5 VS 6 hours (P = 0.02) with ruptured membranes 8.8 VS 8.5 hrs (P = 0.83) and with intact membranes, 19.6 VS 13.1 hours (P = 0.005).

5) Kraines RL et al (1997) reported the induction to delivery interval was significantly shorter (588 verses 885 minutes) in misoprostol verses oxytocin induced patients.

6) Wing D.A. et al (1998) compare the safety & efficacy of vaginally administered misoprostol with the use of intravenous oxytocin for cervical

ripening and labour induction & prior caesarean delivery. Disruption of the uterine incision was found in two women treated with 25 μg of misoprostol.

7) Stitely M.L. et al (1999) reported the time from initial dose of misoprostol to delivery was significantly shorter i.e. 36.9 ± 3.8 hour compared with 61.3 ± 3.8 hour $P < 0.001$ in placebo group.

8) Fernandez E and vavilals S (2000) Reported that After using 50 mg of misoprostol vaginally every four hour, the average induction delivery interval was 10.34 ± 1.14 hours.

The incidence of side effects with both the groups was not very significant and in majority the side effects were tachycardia, hyper systole & tachysystole, fever & Nausea.

Total dose requirement :-

Total dose required in 25 mg misoprostol group was 100 mg (about 4 doses) and 150 mg in 50 mg misoprostol group.

Summary and Conclusion

SUMMARY AND CONCLUSIONS

Induction of labour is the nonspontaneous initiation of uterine contraction that result in progressive cervical effacement and dilation with descent of presenting part. Labour induction should not be attempted unless there are sound obstetrics grounds for expediting the termination of pregnancy.

Elective induction may be successfully and safely performed when the pelvic score totals 9 or more **(Bishop 1964).**

Unfortunately women too frequently have indication of induction of labour with unripe cervix. Prostaglandin preparations have been found to be beneficial in cases with unfavourable cervices (Kerise, 1993).

Recent development of misoprostol, a synthetic prostaglandin E_1 analogue, originally manufactured for prevention and treatment of NSAIDS induced ulcers, has made the induction of labour easier even in cases with unfavourable cervices. Misoprostol act by selective binding to EP_3/EP_2 prostanoid receptor ($EP_3 > EP_2 > EP_1$) (Asboth 1996).

Misoprostol is extensively absorbed and undergoes rapid desterification to its active metabolite misoprostol acid which is responsible for its clinical activity. It has uterotonic and cervical ripening property.

Vaginally administered misopcostol has three times the bioavailability of oral route and is associated with minimal systemic side effects.

In pregnant women being induced with misoprostol abnormal uterine contractions such as tachysystole, hypersystole and uterine hyperstimulation syndrome may occur.

The present study, a comparative study, was undertaken to evaluate the effect of vaginal misoprostol on cervical ripening and labour induction at term, to note induction active labour interval, induction delivery interval, labour complications and preinatal outcome. The results were compared with intravenous oxytocin infusion.

The present study, an observation based study, was carried out on 260 pregnant women of 18-35 years age group with singleton pregnancy of 36-42 weeks, cephalic presentation, no contraindication to vaginal delivery and no history of previous caesarean delivery or any uterine scar.

The study was conducted on an inpatient basis in Maharani Laxmi Bai Medical College, Jhansi Department of Obstetrics and Gynaecology, during the period of one year from 2003 - 2004.

A detailed history was elicited regarding age, parity, habitat, socio-economic status, education, dietary and personal habits with special reference to obstetric history of present, and past pregnancy, duration of gestation and any associated complaint. Thorough general and obstetric examination was done. Per speculum examination was done to note any discharge or leaking per vaginum which was followed by per vaginal examination for assessment of Bishop Score, membrane and pelvis.

Baseline investigations were carried out. The cases were divided into 3 groups. Group I comprised of 80 cases who received 25 microgram misoprostol 3 hourly. Group II included 80 patients where induction was done with 50 microgram misoprostol 6 hourly. Maximum total dose used

in both groups (group I & II) was 200 microgram. Hundred cases in group III were induced with intravenous oxytocin infusion.

Labour was monitored and the observations were made on the basis of age, parity, socio-economic status, education, period of gestation in weeks, preinduction Bishop score, induction active labour interval, induction delivery interval, mode of delivery, maternal and foetal outcome.

Any side effect of the drug was also noted.

The observation and conclusions drawn from this study were as follows ;

1 The age distribution of patients varied from 18-35 years. Maximum number of cases were young belonged to 21 to 25 years age group (52.08%).

2 Out of all cases induced more than half were primigravidae, i.e. 51.25% in group I, 52.5% in group II and 54% in group III.

3 About half of the antenatal cases in all 3 groups were unbooked i.e. 48.75% in group !, 55% in group II and 52% in group III. The percentage of booked cases was 51.25 % in group I, 45 % in group II and 48 % in group III.

4. More than half cases in all 3 groups i.e. 53.75% in group I, 57.5% in group II and 56% in group III were rural dwellers whereas 46.25 % subjects in group I, 42.5 % in group II and 44 % in group III were from urban background.

5. More than half of the cases were either illiterate or had only primary education, i.e. 56.25% in group I, 62.5% in group II and 52.0% in group III. Rest were educated upto high school, intermediate or were graduate.

6. Majority of cases belonged to lower middle socio-economic class i.e. 55% in group I, 47.5% in group II and 56% in group III.

7. In majority of patients in all 3 groups, the period of gestation at which labour was induced, ranged between 37 to 40 weeks i.e. in 75% cases in group I, 77.5% in group II and 64% in group III.

8. In majority of cases in all 3 groups the indication for induction of labour were pregnancy induced Hypertension, postdated pregnancy, prelabour rupture of membrane and term pregnancy i.e. 91.25% in group I, 90.08 % in group li, 96.00% in group III.

9. In more than half of the antenatal cases preinduction Bishop Score was unfavourable (< 5).

10. 48.75% cases in group I, 52.50% cases in group II reached in active labour within 6 hours compared to 20% induced with intravenous oxytocin infusion.

11. In primigravidae mean induction active labour interval was 7.97 ± 4.76 hours in group I, 8.24 ± 5.59 hours in group II and 12.33 ± 6.08 hours in group III. In multigravid subjects it was 5.46 ± 3.52 hours in group I, 6.31 ± 3.82 hours in group II and 12.78 ± 6.10 hours in group III. The induction active

labour interval was less in both primigravidae and multigravidae in misoprostol group compared to oxytocin group. Induction active labour interval was more in cases with unfavourable preinduction Bishop Score than with favourable Score.

12. In primigravidae, induction delivery interval was 9.21 $\pm$ 4.15 hours in group I and 9.28 $\pm$ 4.53 hours in group II compared to 15.66 $\pm$ 5.14 hours in group III. In multigravidae, it was 6.84 $\pm$ 4.41 hours in group I, 6.78 $\pm$ 4.01 hours in group II and 13.11 $\pm$ 7.28 hours in group III. The average induction vaginal delivery interval was much shorter in misoprostol groups than oxytocin group.

13. There was no significant difference regarding mode of delivery in all 3 groups. It was found that 90.6 % patients in misoprostol group and 83% cases in oxytocin group had spontaneous vaginal delivery.

14. Indication for caesarean section in maximum number of cases in all 3 groups was foetal distress.

15. Uterine tachysystole occurred in 2.5% cases in 25 microgram, 7.5 % cases in 50 microgram group and 4 % cases in oxytocin group. Past partum haemorrhage occurred in 2.5 % cases in group I and 4 % cases in group III. Regarding maternal complications there was no significant difference in both misoprostol and oxytocin group.

16. There was no difference in incidence of feotal distress in all the 3 groups. Icterus was observed in 5% cases in oxytocin group.

17. Most of the babies in group I (93.75%), group II (88.75%) and group III (86%) had Apgar Score at 1 minute between 7-10. Apgar score was 0-3 in cases where induction was done for intrauterine foetal death and congenitally malformed foetus incompatible with life. After 5 minutes none of the baby of all the 3 groups had Apgar score 4-6.

18. Most of the babies of all 3 groups had birth weight between 2-3 kg.

19. Systemic side effects of the drug (misoprostol) were minimal. Nausea / vomiting occurred in 2 women (2.5%) in group I, 3 women (3.75%) in group II and 3 women (3%) in group III. Fever occurred in 1.25%, 1.25% and 2% cases in group I, II, III respectively.

20. In misoprostol group, 25 microgram 3 hourly dosage regimen was found to have comparable efficacy as 50 microgram 6 hourly dosage regimen and was associated with minimal incidence of uterine tachysystole and foetal distress compared to 50 microgram group.

In present study, it was noticed that induction active labour interval and induction delivery interval was remarkably shorter in misoprostol groups (Group I & II) compared to oxytocin group (Group III). But there was no significant difference in the mode of delivery, maternal and foetal outcome in both misoprostol and oxytocin groups.

So from above study it can be safely concluded that misoprostol tablet is a promising new prostaglandin for labour induction. It is stable at room temperature, does not need careful storage and confinement to bed is

not necessary. As it is applied locally there are minimal systemic side effects. It is an effective cervical ripening agent in cases with unfavourable cervix. It significantly shorten induction active labour and induction delivery interval with no untoward maternal or fetal events and no increase in instrumental deliveries or caesarean section rate compared to oxytocin.

Even in misoprostol group, in 25 microgram 3 hourly dose regime, there were less incidences of uterine tachysystole and foetal distress compared to 50 microgram 6 hourly dosage regimen. Efficacy of both groups of misoprostol, regarding reduction in induction active labour interval and induction delivery interval and mode of delivery was comparable.

At present misoprostol is the most effective drug for labour induction even in cases with unfavourable cervices as it is safe, reliable, convenient and economic method without untoward effect on mother and foetus compared to oxytocin.

So it can be said that this small wonder has generated a ray of hope in the process of labour induction even in the presence of unfavourable cervix but more studies are required to optimize the dose of misoprostol.

Best is yet to come, tomorrow

What we do today as best

Is only the better of yesterday.

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